VOLUME 14 NUMBER 2

ENDOCRINOLOGY

THE BULLETIN OF THE ASSOCIATION
FOR THE STUDY OF

INTERNAL SECRETIONS

EDITORS

R. G. HOSKINS, Boston

M. O. LEE, Boston H. LISSER, San Francisco

MARCH-APRIL

1930

PUBLISHED BI-MONTHLY BY THE ASSOCIATION FOR THE STUDY OF INTERNAL SECRETIONS, SUITE 1214 WILSHIRE MEDICAL BLDG., LOS ANGELES, CALIFORNIA
ANNUAL SUBSCRIPTION, $6.00 SINGLE COPIES, $1.25

At the Menopause

The distressing symptoms that so often accompany the climacteric, but more particularly the aggravated symptoms of the artificial menopause, are frequently controlled by the administration of

LUTEIN TABLETS, H. W. & D.
LUTEIN SOLUTION AMPULES, H. W. & D.

The choice of the medication depends, of course, on the judgment of the physician as to whether oral or hypodermatic administration is indicated. Both products represent the

CORPUS LUTEUM OF THE SOW

Lutein Tablets H. W. & D. are unmodified by treatment with solvents or by exposure to temperatures above animal body heat in the drying process. All separation of extraneous matter is made by mechanical means and all drying is in vacuo. The unaltered corpus luteum should, therefore, be presented in our products and clinical experience with them should demonstrate their therapeutic activity.

Ovarian dysfunction as evidenced in dysmenorrhea and amenorrhea is also an indication for Lutein medication. Where the diagnosis of such dysfunction was well established, definite therapeutic results have been reported.

WHOLE OVARY TABLETS, H. W. & D.
OVARIAN RESIDUE TABLETS, H. W. & D.

are also offered for those who prefer, for certain indications, the use of the whole gland or of the residue remaining after corpus luteum separation.

Literature furnished on request

H. W. & D.—SPECIFY—H. W. & D.—SPECIFY—H. W. D. SPECIFY—H. W. & D.

HYNSON, WESTCOTT & DUNNING

BALTIMORE, MD.

ENDOCRINOLOGY

THE BULLETIN OF THE ASSOCIATION FOR THE STUDY OF

INTERNAL SECRETIONS

Volume 14, Number 2 MARCH-APRIL, 1930 Serial No. 70

OVARIAN HORMONE EFFECTS IN OVARIECTOMIZED MONKEYS

D. C. ROBERTSON, W. P. MADDUX AND E. ALLEN

Department of Anatomy, University of Missouri[1]

COLUMBIA

In earlier experiments reported from this laboratory effects of ovarian and placental extracts[2] upon adult and immature monkeys have been described (Allen, 1, 2, 3). This work has demonstrated first, that the reddening and swelling of the "sexual skin" and also the growth which normally occurs in the genital organs and mammary glands during the first half of the menstrual cycle may be induced by administration of this hormone and, second, that experimental menstrual periods follow cessation of injections of hormone in a majority of ovariectomized monkeys.

In the above experiments, however, full pre-menstrual development of the glands of the endometrium was not obtained. Consequently it appeared that the experimental menstrual periods in these ovariectomized animals corresponded more nearly to those occurring in normal monkeys in the absence of ovulation (Van Herwerden, 4, and Corner, 5). It seemed desirable therefore to continue the experiments with increased dosages of hormone in an attempt to ascertain the extent of growth of endometrial structures possible with these extracts. One series of hormone experiments was planned in which implants of recent corpora lutea were made toward the end of a series of injections of hormone. An additional point of interest which has been followed in this work has been a determination of the glycogen content of the epithelium of the vagina and uterus during experimental menstrual cycles. Corner's work (6) provides a control on this aspect of the problem in normal monkeys.

Following the demonstration of this active principle of ovaries and placenta in the urine of pregnant women (7, 8) it was decided to make analyses of the urine of injected animals to see what percentages of the injected hormone might be recovered during the course of the experiments.

Four female monkeys which had been under observation for seven months were used in these experiments. Where possible ovariectomy was

1. This work has been assisted by grants from the Committee for Research in Problems of Sex of the National Research Council.

2. Names such as "follicular hormone," "folliculin," "oestrous producing hormone or oestrin," "estrogen," "menformon," "amniotin" have been used for active extracts of the ovary and placenta which have been standardized by the rat test—the production of full oestrous growth in the genital organs of ovariectomized rats.

performed between the 10th and 16th days following onset of the previous menses. Following ovariectomy periods of atrophy from 66 to 104 days elapsed before the beginning of injections. Before injections were begun each animal was operated upon again, the uterus measured and one uterine tube and mammary gland removed for controls. At this time a clipping from the fimbriated end of each control tube was examined in warm Ringer's solution for motility of cilia. The nipples were cut from the control mammary glands and sectioned. The rest of the mammary glands were prepared as flat mounts for the study of the size and number of the ducts and alveoli.

There followed a period from 20 to 33 days between the second operation and the beginning of injections in which it is probable that additional retrogression occurred in the genital organs.

The animals were injected two or three times daily as nearly at twelve or at eight-hour intervals as possible. Injections were made alternately into each hind leg. Handling the monkeys was facilitated by running them from a large cage into a small trap cage.

Following ovariectomy and during the course of control periods, the extent of coloring and swelling of the "sexual skin" was noted. Changes were followed in the contents of vaginal smears—especially the proportion of leucocytes to epithelial cells and to erythrocytes and the glycogen content of the epithelial cells.

Urine was collected for periods ranging from overnight (16-hour samples) to 24 hours. A simple method of extraction of hormone outlined by Doisy was used. This consisted of a thorough shaking of the urine samples with from 3 to 10 cc. of olive oil (depending upon the amount of urine). The oil was then removed in a separatory funnel. It is realized that this was not a thorough quantitative extraction but with reasonable precautions as to standardization it was sufficiently accurate for our purposes. The hormone content was tested by injection into ovariectomized adult rats as previously described and the results expressed in rat units.

The menstrual history of the four monkeys after ovariectomy follows. Animal SR began to menstruate on the third day after the removal of the ovaries, the duration of operative menses being three days. Animal SRS began to menstruate on the fifth day following ovariectomy; the duration of menses was two days. Animals SB and SLS did not experience operative menses. These results may be added to a similar series previously reported (9).

Following ovariectomy the reddening and swelling of the "sexual skin" decreased and slowly disappeared and leucocytes entered the masses of cells in the vaginal lumen.

Several types of extracts[3] were injected. One was a lipoid extract of human placenta dissolved in olive oil. A second (Amniotin, Squibb) was

3. We wish to acknowledge the generous cooperation of Doctor A. W. Lescohier of Parke Davis Company and Doctor John F. Anderson of E. R. Squibb & Sons in furnishing these extracts.

a water preparation containing 10 rat units per cc. A third (Estrogen, Parke Davis) was a water preparation containing 25 rat units per cc. A fourth (Lipo-lutein, Parke Davis) was a lipoid extract of corpus luteum prepared by similar extraction methods but not standardized by biological assay. In addition to these extracts implants of fresh corpora lutea from human subjects who had ovulated recently were implanted toward the end of the experiment in two animals. These corpora lutea[4] were removed between the 15th and 24th days of the menstrual cycle and consequently contained considerable amounts of active material (Allen, Pratt, Newell and Bland, 10).

Animal SR was ovariectomized on July 24th. Injections were begun on October 19th, 86 days after ovariectomy. A total of 447 rat units of lipoid extract of human placenta in oil solution was injected over a period of 48 days. Dosage began with 1.5 rat units per day and was gradually increased to a maximum of 25 rat units per day on the last day of injections. The animal was killed the day following the last injection and the genital organs examined histologically.

Toward the end of the first week of injections the colorless "sexual skin" of the ovariectomized animal reddened and then gradually deepened until a maximum redness was obtained by the end of the experiment. There was no swelling of the skin of these regions. Leucocytes were completely absent from the vaginal smears after the first two weeks of injections and the number of cornified cells increased rapidly. Since the animal was killed the day following the last injection, too soon for the occurrence of menses, the experiment deals only with the anabolic phase of the menstrual cycle.

The above experiment was designed to imitate conditions which sometimes exist in normal animals where periods of two or three months of amenorrhea may occur (1). That the ovaries of such animals are actively secreting this hormone is shown by the reddening of the "sexual skin." The ovaries in such cases usually have several follicles (occasionally one or two cystic ones) but no corpora lutea. In the above experiment therefore it is interesting that no menstruation occurred during continuous hormone stimulation sustained for forty-eight days.

A second series of injections were made into three animals, SLS, SB and SRS, beginning on November 5th. Before beginning injections and after periods of from 83 to 91 days following double ovariectomy the animals were opened, uteri measured and one tube and one mammary gland removed from each for controls. Control smears were taken of the vaginal contents. Control measurements of the uterus are listed in table I and the conditions of the tubes and mammary glands will be discussed under histological findings. In the vaginal smears of the controls considerable numbers of leucocytes were present (Fig. 1) and it was not possible to demon-

4. These corpora lutea were enucleated from ovaries at operations by Doctor J. P. Pratt of the Henry Ford Hospital, Detroit, and Doctor Q. U. Newell of Barnes Hospital and Washington University, St. Louis.

strate the presence of glycogen in the epithelial cells. The period of injections lasted from 24 to 27 days. For the first 13 days two injections were given at 12-hour intervals. During the remainder of the experiment three injections a day were made at approximately eight-hour intervals. A total of 886 rat units was injected into animal SLS, 981 rat units into animals SB, and 882 rat units into animal SRS.

In animals SLS and SRS one-half of a human corpus luteum was implanted on the 22nd, 23rd and 24th days of injections. The human corpora used were cut into small pieces to facilitate absorption of any hormone specific for the corpus luteum which might be already present in them. In animal SB from the 22nd to 27th days injections of "lipo-lutein," a

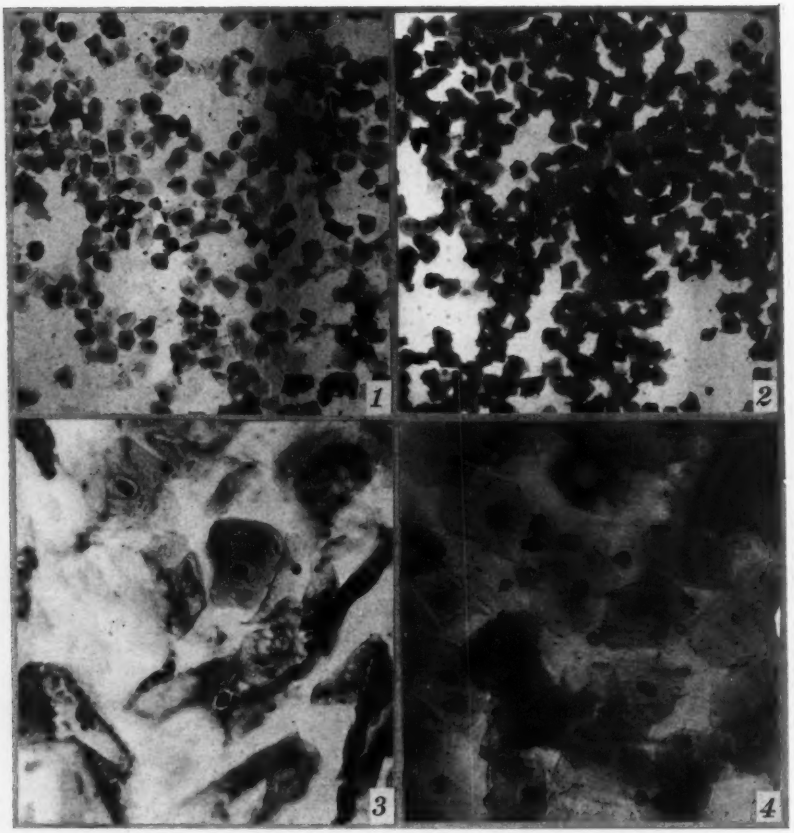

Fig. 1. Cells from the vaginal lumen of an ovariectomized control monkey. Partly cornified epithelial cells with pycnotic nuclei and varying numbers of leucocytes. X 50.

Fig. 2. Cornified epithelial cells from the vaginal smear toward the end of a series of injections. Leucocytes are absent. X 50.

Fig. 3. Glycogen granules in epithelial cells from vaginal smear of monkey SLS toward the end of a series of injections of hormone. X 294.

Fig. 4. Cells of vaginal smear of monkey SRS during an experimental menstrual period. Nucleated epithelial cells, a few leucocytes and erythrocytes. X 220.

lipoidal extract of corpus luteum, were administered. This corpus luteum implant and extract were administered at the same time that the follicular hormone was being given because it has been demonstrated that the human corpus luteum during the last half of the menstrual cycle contains large amounts of this hormone (10) as well as other active substances possibly specific for the corpus luteum (11, 12, 13).

By the end of the first week of injections reddening of the "sexual skin" appeared. This deepened by the end of the second week and before the end of the period of injections was reached had attained a maximum coloration. In animal SLS an extreme amount of swelling of this skin occurred. In the other two animals the swelling was not so marked.

The leucocytes disappeared from the smear by the middle of the second week of injections. Toward the latter half of the experiment large amounts of mucus appeared in the vaginal contents. There was a marked increase in the number and in cornification of the epithelial cells (Fig. 2). During the last week of injections glycogen could be demonstrated in the epithelial cells of the smear (Fig 3).

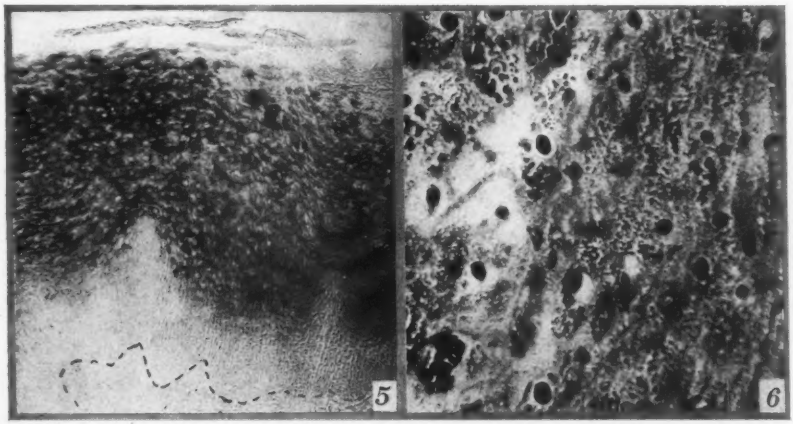

Fig. 5. Vaginal wall of animal SR toward the end of a series of injections. This section was stained with Lugol's iodine for a demonstration of glycogen. The dotted line indicates the germinal layers of the epithelium. It will be noted that most of the glycogen is in the outer degenerating cells. X 75.

Fig. 6. A small section of the vaginal wall of monkey SLS stained with Best's carmine to show glycogen content of epithelial cells. X 440.

Animal SLS was killed on the last day of injections, too soon after cessation of injections to permit the appearance of menses. Animal SB was killed on the third day following the last injection. Although no menses were visible externally, when the genital tract was removed and opened an early menstrual condition was found, the lumen of the uterus and inner part of the vagina being filled with menstrual material. Animal SRS was killed on the second day following the last injection. At this time menses were apparent externally and this condition was checked by smears (Fig. 4) and by gross and histological examination.

A gross examination of the genital organs of these three monkeys at autopsy showed the following points. A thick, white accumulation of material was found in the vaginal lumen. This was composed of sloughed epithelial cells and mucous discharged from the cervical glands. In addition, in the two animals already noted the endometrium was hemorrhagic and menstrual discharge was present. The endometrium of animal SB, killed on the first day after the last injection, was a pale white color.

In the three animals of the last series measurements were taken of the uterus at the time of ovariectomy, at a control operation before injections were begun and again at the end of the series of injections. These measurements are included in Table I. These figures show a considerable decrease in size due to castration atrophy but a complete recovery to equal or exceed the size of the normal uterus following injections.

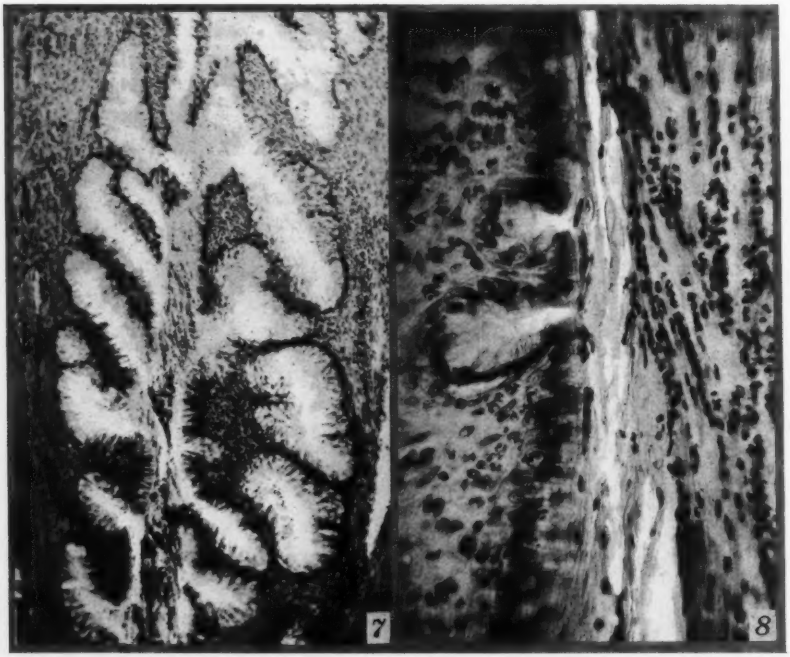

Fig. 7. A section of a gland from the external os of the cervix in a hypertrophied condition at the end of a series of injections. X 44.

Fig. 8. A higher magnification from the same gland showing a high columnar epithelium and many leucocytes in the stroma, in the epithelium and in the gland lumen. X 200.

Histologic sections of the vaginal wall confirmed conclusions drawn from earlier experiments as to extremely rapid growth of the epithelium (1). The extreme thickness to which the vaginal wall can be developed, especially when compared to the control condition after castration atrophy, is surprising.

The presence of glycogen was demonstrated in sections of the vaginal wall from all three animals of the last series (Figs. 5 and 6). It was scarce, if present at all, in the vaginal epithelium of the control animal.

In the animals in which a day or two elapsed between the last injection and death of the animal, leucocytic infiltration of the lower layers of the epithelium had begun.

TABLE I
TABLE OF UTERINE MEASUREMENTS

Time of Measurement	Monkey		
	SRS	SB	SLS
At ovariectomy	12 x 8 mm.	13 x 10 mm.	9 x 7.5 mm.
Just before injections (Atrophy 66–104 days)	10 x 5.6 mm.	11 x 5.6 mm.	9 x 5.5 mm.
At end of injections	12 x 9 mm.	12 x 5.6 mm.	15.5x 9 mm.

The cervices of the injected animals were considerably hypertrophied. The glands near the external os were tremendously enlarged and coiled (Fig. 7). The epithelium was high columnar. Secretion by these glands was active as shown by secretion droplets along the free borders of the

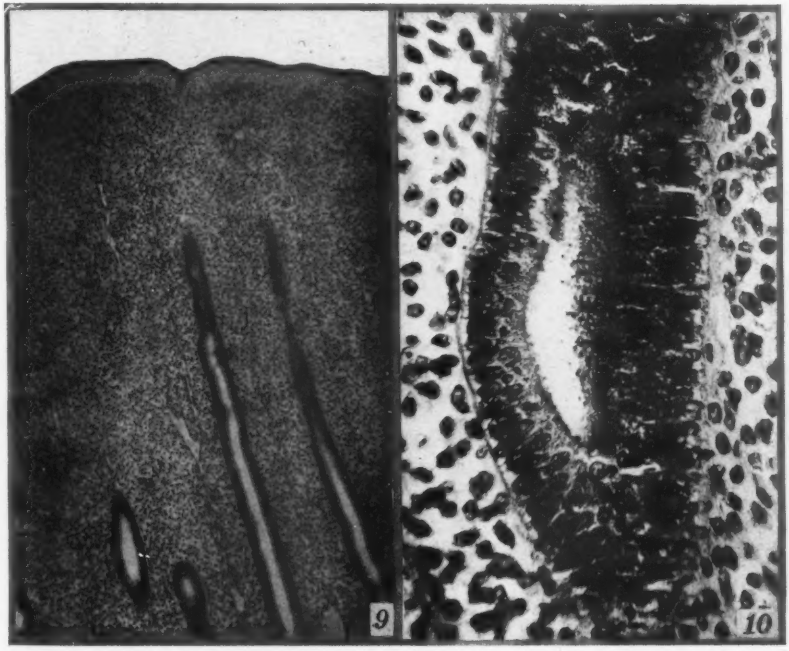

Fig. 9. A section of the uterus of monkey SLS killed on the last day of injections. This is a typical interval type of endometrium. Hyperplasia in the gland epithelial is at its height. X 50.

Fig. 10. Higher magnification of one of the glands in the same endometrium stained with Best's carmine to show glycogen granules in the glandular epithelium and lumen. X 298.

cells. The stroma surrounding the glands was heavily infiltrated with leucocytes and many of these could be traced into the lumen of the gland (Fig. 8). A few small glycogen granules were also present. This leucocytic infiltration in the cervical glands under the influence of ovarian hormone is as yet unexplained. It has been present in all of our monkeys

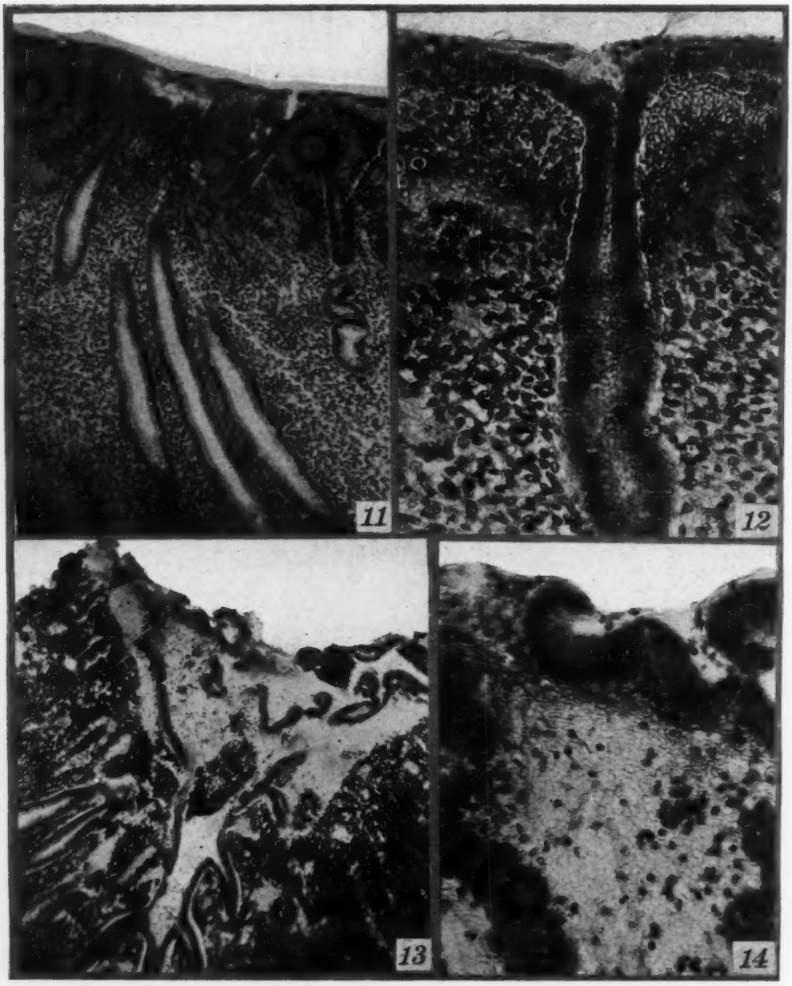

Fig. 11. Section of endometrium of animal 8B, killed on the third day after the last injection. The glands had not reached typical premenstrual development. The sub-epithelial stroma was edematous and extravasation of blood had begun. X 50.

Fig. 12. Higher magnification of endometrium from the same animal showing the sub-epithelial hematoma. X 220

Fig. 13. Section of endometrium from animal 8RS on the second day after the last injection. This was a later menstrual stage in which the superficial layer was being sloughed. X 40.

Fig. 14. Higher magnification of the menstrual material in the lumen of the uterus showing pieces of glands, erythrocytes and polymorphonuclear leucocytes. X 133.

Sections of the uterine tubes from control and injected animals.

under hormone stimulation. The question arises if this may be a physiological leucorrhea.

For comparison with the uteri from injected animals there was one control uterus from monkey SB removed after a period of 66 days of castration atrophy. This uterus was small (12x7 mm.) and anemic. The

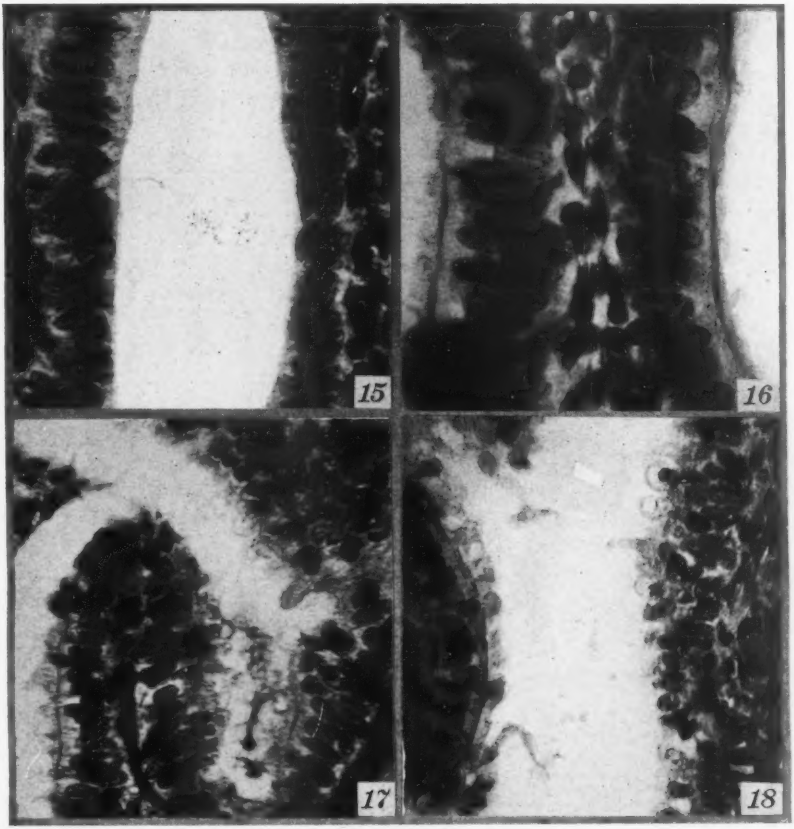

Fig. 15. Non-ciliated epithelium from control tube of animal SB, 84 days after ovariectomy. X 710.

Fig. 16. Epithelium from the other tube of the same animal at the end of injections. Note high columnar structure and regeneration of cilia. X 710.

Fig. 17. Tubal epithelium of animal SR at the end of injections. X 330.

Fig. 18. Another section of epithelium from the same tube. X 330.

endometrium was thin and compact. The surface epithelium was degenerate and contained no mitotic figures. The glands were few and poorly developed. Glycogen was present in the epithelial cells of the glands in traces only.

Of the four uteri removed following injections, two (from animals SR and SLS) had endometrium of the interval type as far as gland devel-

opment was concerned (Fig. 9). The superficial stroma was very loose meshed and edematous. Many mitotic figures were present in the superficial epithelium and glands. Secretion globules were present in the gland lumina and along the outer borders of the cells. Glycogen granules were very abundant in both the cells of the glands (Fig. 10) and the superficial epithelium. It is probable that the corpus luteum extract and implants were not continued for a period sufficient to carry gland development beyond the interval stage because Corner and W. Allen (12) and Hisaw (13) have reported pseudo-pregnant and premenstrual conditions of uterine glands in the rabbit and monkey, respectively, due to corpus luteum extract.

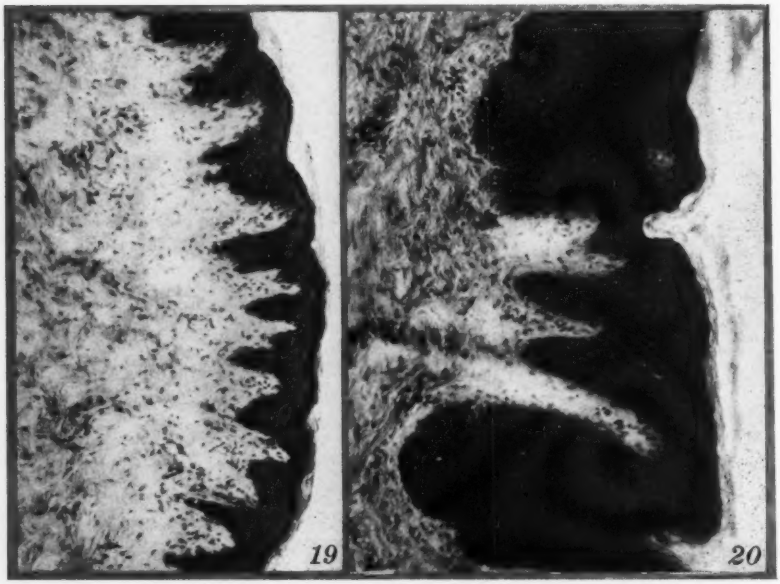

Fig. 19. Section of epithelium of the nipple from control gland of animal SRS 53 days after double ovariectomy. X 100.

Fig. 20. Epithelium from the other gland of the same animal at the end of a period of injections. X 100.

The other two uteri (from animals SRS and SB) were in a typical early menstrual condition. The endometrium was thicker than the control; the glands as would be expected at an early menstrual stage were not very well developed. Sheets of superficial epithelium and adjacent stroma had been loosened and cast off and menstrual blood was present both under the epithelium and in the lumen of the uterus (Figs. 11, 12, 13 and 14). The incidence of mitosis was not high and only small amounts of glycogen could be demonstrated in the epithelial cells.

The epithelium of the left uterine tubes which were removed for control specimens was relatively low and cilia were few or absent (Fig. 15).

Motility of cilia could not be demonstrated in small pieces of the fimbriated ends examined in warm Ringer's solution. Small round cells were scattered abundantly throughout the epithelium close to the basement membrane. Only small amounts of glycogen were demonstrable.

The epithelium of the right uterine tubes removed after injections was in marked contrast to that of the controls. It was higher and better ciliated (Figs. 16, 17 and 18). Motile cilia were observed in fresh preparations. The small round cells next to the basal membrane were much more scarce than in the control tubes. A high incidence of mitoses was indicated and glycogen granules were fairly abundant in the epithelial cells. A remarkable recovery from atrophy following ovariectomy was apparent.

In studying injection effects on the mammary glands the left gland from each animal was used for a control and the right for an experimental specimen. The epidermis of the nipples of the control glands was not very thick, being composed of from three to twelve layers of nuclei (Fig. 19). It was difficult to identify mitoses. The epithelium of the nipples after injections was much thicker; there were 27 layers of nuclei in the thickest specimen and with a thick stratum cornium in addition (Fig. 20). Mitoses were abundant in the germinal layers.

The mammary glands after injections were considerably larger than the controls; the ducts longer, larger and more branched and having more alveoli. This phase of the work is well illustrated in an earlier publication (1).

The condition of the luteal tissue which was placed in subcutaneous pockets in these monkeys was interesting. This tissue was heavily infiltrated with leucocytes and for the most part not recognizable as luteal tissue. In two implants, however, which had been in the hosts four and six days, respectively, small areas of apparently normal luteal tissue could still be identified.

A total of nineteen samples of urine was analyzed from monkeys SB, SLS and SRS during the course of injections. During the collection of the samples injections were made three times daily at approximately eight-hour intervals, the daily dose ranging from 18 to 58 rat units. Analyses of nine samples from spayed animals before injections were made for controls and in none was enough hormone obtained to give a positive rat test. The amount of hormone recovered from the urine of injected animals ranged from 12.9 to 57 per cent of the hormone injected, the average being 29.3 per cent.

SUMMARY

Ovarian hormones were injected into four ovariectomized adult female monkeys. In two corpora lutea also were implanted. Two experimental menstrual periods followed cessation of injections of oestrous-producing ovarian hormone. Sections of the uteri showed typical menstrual endo-

metria of the non-ovulating type. Three implants of recent human corpora lutea did not increase the growth of the endometrial glands beyond the interval stage.

Toward the end of the series of injections it was possible to demonstrate the presence of considerable amounts of glycogen in the epithelial tissue of the uterus and vagina. Glycogen was relatively scarce in the control tissues. Glycogen could also be demonstrated in the epithelial cells sloughed from the vaginal wall. In the vagina it increased in amount as cornification of epithelial cells progressed.

The epithelial lining of the uterine tubes of the injected animals showed remarkable recovery from atrophy following ovariectomy. Mitotic division of cells and regeneration of cilia in some regions were demonstrated. Extensive growth was also induced in the mammary glands, including the skin of the nipples.

Considerable amounts of the hormone injected were recovered from the urine of experimental animals.

BIBLIOGRAPHY

1. Allen, E.: The menstrual cycle of the monkey, Macacus rhesus: Observations on normal animals, the effects of removal of the ovaries and the effect of injections of ovarian and placental extracts into the spayed animals. Contrib. to Embryol., Carnegie Inst., Wash. Pub. No. 380, **19:** 1. 1927.
2. Allen, E.: Further experiments with an ovarian hormone in the ovariectomized adult monkey, Macacus rhesus, especially the degenerative phase of the experimental cycle. Am. J. Anat. **42:** 467. 1928.
3. Allen, E.: Reactions of immature monkeys to injections of ovarian hormone. J. Morph. & Physiol. **46:** 479. 1928.
4. Van Herwerden, M.: Beitrag zur Kenntnis des menstruellen Cyklus. Monatschr. f. Geburtsh. u. Gynäk. **24:** 730. 1906.
5. Corner, G. W.: The relation between menstruation and ovulation in the monkey. J. A. M. A. **89:** 1838. 1927.
6. Corner, G. W.: Ovulation and menstruation in Macacus rhesus. Contrib. to Embryol., Carnegie Inst., Wash. Pub. No. 332, **15:** 75. 1923.
7. Loewe, S and F. Lange: Der Gehalt des Frauenharnes an brunsterzeugengenden Stoffen in Abhangigkeit vom ovariellen Zyklus. Klin. Wchnschr. **5:** 1038. 1926.
8. Veler, C. D. and E. A. Doisy: Extraction of ovarian hormone from the urine. Proc. Soc. Experi. Biol. & Med. **25:** 806. 1928.
9. Allen, E.: Effects of ovariectomy upon menstruation in monkeys. Am. J. Physiol. **75:** 471. 1928.
10. Allen, E, J. P. Pratt, Q. U. Newell and L. B. Bland: Hormone content of human ovarian tissues. Am. J. Physiol. **92:** 127. 1930.
11. Papanicolaou, G. N.: A specific inhibitory hormone of the corpus luteum. J. A. M. A. **86:** 1422. 1926.
12. Corner, G. W. and W. M. Allen: Production of a special uterine reaction by extracts of the corpus luteum. Am. J. Physiol. **88:** 326. 1929.
13. Hisaw, F. L. and S. L. Leonard: Relation of the follicular and corpus luteum hormones in the production of progestational proliferation of the rabbit uterus. Am. J. Physiol. **92:** 574. 1930.

ANTERIOR LOBE PITUITARY SUBSTANCE AND BASAL RESPIRATORY METABOLISM

MILTON O. LEE AND JULES GAGNON
The Memorial Foundation for Neuro-Endocrine Research,
Harvard Medical School
BOSTON, MASS.

Despite a considerable amount of negative and very little positive evidence as to the efficacy of anterior lobe substance when administered by the alimentary tract, such therapy is nevertheless extensively used. The most of the carefully controlled experimental work (1, 2, 3, 4, 5) on feeding this material to dogs, cats, rats and mice has shown it to be entirely without effect on general bodily or genital growth and development. The few positive results on mammals that have been reported are largely equivocal and have been derived from poorly controlled experiments on an insufficient number of animals. Reports both of stimulation and inhibition of growth and development have been made. Patterson (6) in a recent paper has summarized this experimental work.

Clinically, anterior lobe substance by mouth has been used in cases diagnosed as "hypopituitarism," "hypo-anterior lobe," "hypogenitalism" and "infantilism," in cases of obesity, amenorrhea, and of disturbed metabolism which are supposedly not due to thyroid disorders. For the most part only the positive results of such therapy have been reported, but those show a still poorer case for its efficacy, in that the cases have usually been entirely uncontrolled, the anterior lobe preparation has often been used in connection with thyroid or other opotherapy, and the criteria of the results are very superficial.

We have found that extracts of the anterior lobe containing the growth promoting principle when injected parenternally cause a definite lowering of the basal gaseous metabolic rate, both in giant rats (7) and in rats before a condition of gigantism has had time to develop (unpublished work). McCordock (8) has recently reported that the oral administration of desiccated anterior lobe substance to guinea pigs caused a depression in the activity of the thyroid, with a marked lowering of the number of mitoses, the production of only medium sized or small acini with hard colloid compressing the lining epithelium into thin strands. We have observed that in rats injected with the growth promoting principle for some time, the thyroids are grossly smaller in size. It would seem that if anterior lobe substance is at all potent when given by mouth, some effect upon the respiratory metabolism should be produced.

EXPERIMENTAL

Fourteen male albino rats of a pure Wistar strain and approximately six months old at the beginning of the experiment were used. After a

preliminary period of about three weeks, during which at least two satisfactory basal metabolic rate determinations were made for each animal, 8 of the rats were given desiccated anterior lobe substance* for 62 days. This was given each morning, mixed with a little bread and milk, to each rat individually. No difficulty was experienced in getting the animals to eat the mixture. The dosages used were 2 grains of desiccated gland substance per day per rat for 8 days, then 4 grains for 8 days and finally 8 grains per day per rat for 46 days. One grain of the desiccated gland corresponds to about 5 grains of fresh anterior lobe. Each rat at the end of the feeding period had received a total of 370 grains or 24 grams of the dried substance, which might correspond to a relative amount of at least three or four pounds in man. During the feeding period and for several months afterwards frequent basal metabolic rate determinations were made for these rats and for the controls. One of the rats receiving anterior lobe and two of the controls were killed accidentally before the completion of the experiment.

The basal metabolic rate determinations were made by a closed circuit, oxygen consumption method using a four unit apparatus and a technic that has been carefully standardized. Each determination used in the calculations represents the lowest rate measured in several tests over a four to six hour period and 18 to 24 hours after the last ingestion of food. All determinations used were considered satisfactory from a technical standpoint, that is, the starved animals had shown few or no movements during the test, there was no leak in the system and the soda lime tubes showed proper absorption. The metabolic rates are expressed in terms of calories per day per square meter of body surface, which was calculated from the formula

$$S = 10.76\ W^{0.61}\left(\frac{0.31}{\frac{W^{1/3}}{L}}\right)$$

in which W is body weight in grams and L body length in centimeters.

Table I gives a summary of the results. The average metabolic rate for the 8 experimental animals during the preliminary period was 909 calories per day per square meter. Omitting the data for rat 205, which died before the completion of the experiment, the average rate was 900 calories. During this period the four control rats which lived throughout the experiment had an average rate of 891 calories. During the feeding period the experimental rats showed an average metabolic rate of 913 calories, or without No. 205, of 905 calories. The controls during this period had an average rate of 897 calories. During the post-feeding period the 7 rats fed anterior lobe had an average rate of 901 calories and the controls of 900 calories. Figure 1 shows graphically the course of the metabolic rate in each rat.

*Burroughs-Wellcome and Parke Davis Company desiccated anterior lobe pituitary substance was used.

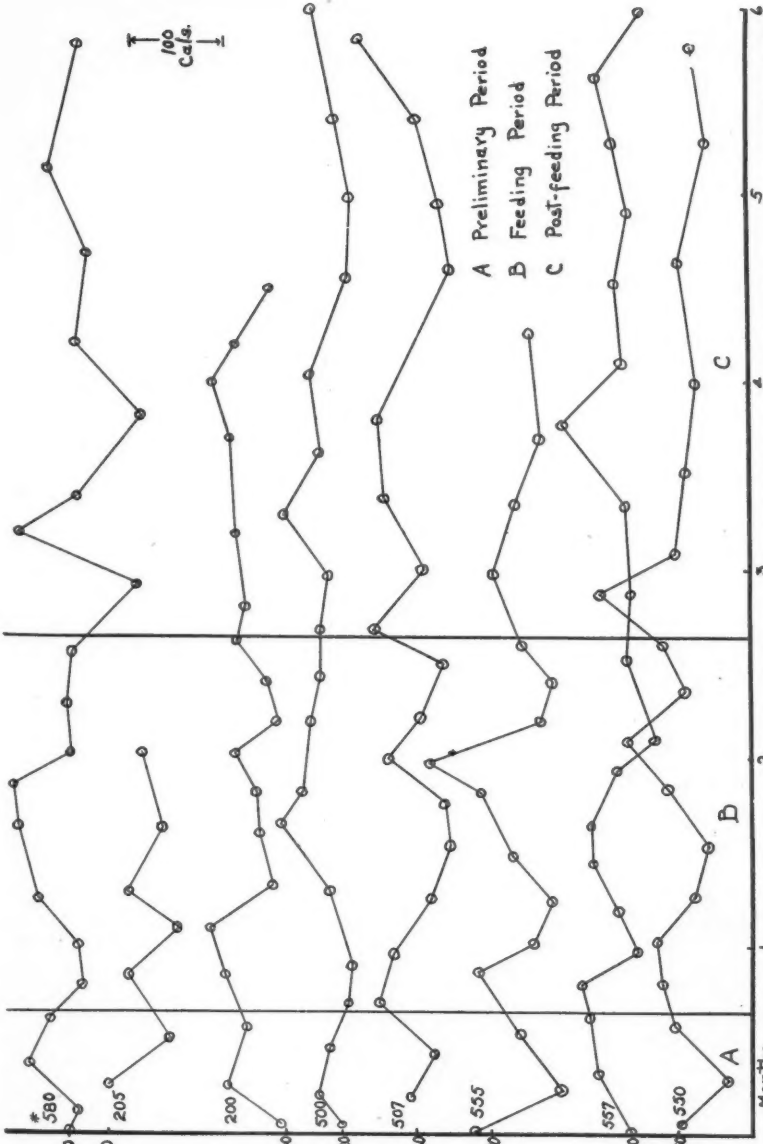

Fig. 1. Basal metabolic rates of individual rats, in calories per day per square meter, before, during and after anterior lobe feeding.

The small differences in the metabolic levels, as given by the averages, are entirely insignificant, and the fluctuations shown in the individual graphs occur equally in control rats. No differential effect of the three dosages is apparent. Respiratory quotients determined at frequent intervals showed no significant deviations from the normal value of approxi-

TABLE I

BASAL METABOLIC RATES BEFORE, DURING AND AFTER ANTERIOR LOBE FEEDING

Rat No.	Preliminary Period			Feeding Period			Post-Feeding Period		
	Weight Range Gms.	No. of Tests	Cals., Day, Sq. M. Average	Weight Range Gms.	No. of Tests	Cals., Day, Sq. M. Average	Weight Range Gms.	No. of Tests	Cals., Day Sq. M. Average
200	296–300	3	936	292–310	9	937	308–316	5	947
205	332–335	2	975	338–353	5	966	.....	..	...
500	322–326	3	932	322–340	7	941	320–342	9	936
507	269–278	2	851	265–294	8	856	280–295	7	873
550	274–276	3	830	278–300	8	854	290–309	7	850
555	257–260	3	949	280–301	9	957	295–309	4	947
557	262–265	3	856	262–270	8	846	270–295	9	844
580	275–278	4	946	282–320	8	945	317–341	8	912

mately 0.72 either during or after the feeding period. While it is true that negative results are not definitely conclusive, it would appear that the preparations of anterior lobe and the dosages used in this work are entirely ineffective in altering the level of metabolic activity.

SUMMARY

Desiccated anterior lobe pituitary substance fed to 8 adult rats in doses of 2, 4 and 8 grains per day per rat for 62 days had no effect on the basal respiratory metabolism or on the respiratory quotient.

BIBLIOGRAPHY

1. Drummond, J. C. and R. C. Cannan: Biochem. J. **16**: 53. 1922.
2. Evans, H. M. and J. A. Long: Anat. Rec. **21**: 62. 1921.
3. Sisson, W. R. and E. N. Broyles: Johns Hopkins Hosp. Bull. **32**: 22. 1921.
4. Smith, C. S.: Am. J. Physiol. **65**: 277. 1923.
5. Smith, P. E.: Am. J. Physiol. **81**: 20. 1927.
6. Patterson, T. L.: Arch. f. Entwcklngsmechn. d. Organ. **113**: 267. 1928.
7. Lee, M. O., H. M. Teel and J. Gagnon: Proc. Soc. Exper. Biol. & Med. **27**: 23. 1929.
8. McCordock, H. A.: Am. J. Pathol. **5**: 171. 1929.

THE RÔLE OF THE ADRENAL MEDULLA IN THE MAINTENANCE OF BLOOD PRESSURE

SWALE VINCENT AND J. H. THOMPSON
From the Dept. of Physiology, Middlesex Hospital, Medical School
LONDON

LITERATURE

Some of the earlier workers investigating the function of the adrenal medulla concluded as a result of their experiments that a constant secretion of adrenaline occurs which helps to maintain the normal blood pressure.

Strehl and Weiss (9), who extirpated the adrenal gland on one side in rabbits, found that when the adrenal vein of the other side was clamped the blood pressure immediately fell, and that there was a recovery when the clamps were released. Marked falls of blood pressure were obtained in this way.

Young and Lehmann (16) working in Vincent's laboratory repeated the experiments upon dogs but found little, if any, fall of blood pressure.

One of the first workers to grow suspicious on this point was Vincent, who was unable to obtain any lowering of blood pressure when the adrenal veins were clamped and a consequent recovery when the clamps were released.

Hoskins and McClure (6) using dogs under various anaesthetics obtained only transitory variations of blood pressure after ligature of the adrenal veins.

Much evidence has been advanced by various workers to militate against the theory that the adrenal medulla is a factor in the maintenance of blood pressure. Moore and Purinton (7) showed that small amounts of adrenaline, such as presumably are liberated normally from the adrenal glands, cause a lowering of the blood pressure. Stewart and Rogoff (8) found that in animals from which one adrenal gland was removed and the secretory fibres from the semi-lunar ganglia on the other side transected, no ill effects were apparent.

More recently, Cannon (3) using the denervated heart preparation has demonstrated the secretion of considerable quantities of adrenaline in the medulla in conditions of stress, and has established the well-known "emergency" theory. Previous investigations by the same worker failed to reveal any adrenaline present in the blood collected from the vena cava and subjected to various physiological tests.

Cramer (4), however, has shown that subjection of an animal to cold for a prolonged period results in exhaustion of the adrenal medulla, and Vincent (11) has demonstrated the same effect after fatigue in rats.

Moreover, the low blood pressure always present in Addison's disease remains to be explained. In this disease the basal metabolic rate is very considerably lowered, and it is significant that in animals after complete adrenalectomy the metabolic rate is reduced by about 25 per cent, and can be raised again to the normal by the injection of adrenaline.

An important contribution to this subject has been made by Bazett (2). Using cats chiefly, this worker attempted to measure the rate of the fall of blood pressure in animals in which the adrenals were removed under ether anaesthesia, under urethane anaesthesia, and in decerebrate animals. All experiments were carefully controlled. Excision of the adrenal glands in the decerebrate animal led to death in about six hours, the pressure beginning to fall about one hour after excision. Control animals showed no falls of blood pressure 28 hours later. Decerebrate preparations developed these changes more quickly than animals anaesthetised. Moreover, animals anaesthetised and allowed to recover failed to manifest such fall of blood pressure. A similar series of results have been obtained recently by Vincent and Thompson (14).

ANATOMICAL CONSIDERATIONS

Cow (5) has indicated the presence of a collateral circulation in the region of the adrenal gland. Vincent and Wright (15) suggested that the persistence of the "dip" in the splanchnic curve after stimulation of the splanchnic nerve under chloralose anaesthesia with the adrenal veins tied, was due to a collateral circulation. Thompson (10) confirmed this, and Vincent and Thompson (13) showed that the effect was exaggerated by chloralose due to the fact that this drug activates the secretion of adrenaline and possibly forms a weak chemical compound more stable than adrenaline, and which sensitises nerve terminals.

Recently Vincent and Thompson (14) have demonstrated in detail the anatomical arrangements of this collateral circulation, which in brief consists of one or more small veins draining the adrenal veins in its course across the gland, into the renal vein, and also a more complicated plexiform group of vessels situated posteriorly.

Therefore, the older experiments in which only the adrenal veins were clamped or ligatured were fallacious, since the adrenaline could still leak through the collateral circulation.

METHODS AND RESULTS

The present series of experiments have been undertaken in order to re-investigate this problem in the light of the new anatomical facts. The experiments have been performed upon cats under various kinds of anaesthetics, and in the decerebrate condition. Anaesthetics used include ether, chloroform, chloralose, luminal sodium, urethane, and different combinations. In all cases the results were identical and the presence or absence of anaesthetic is immaterial to the actual result, although, as will be dem-

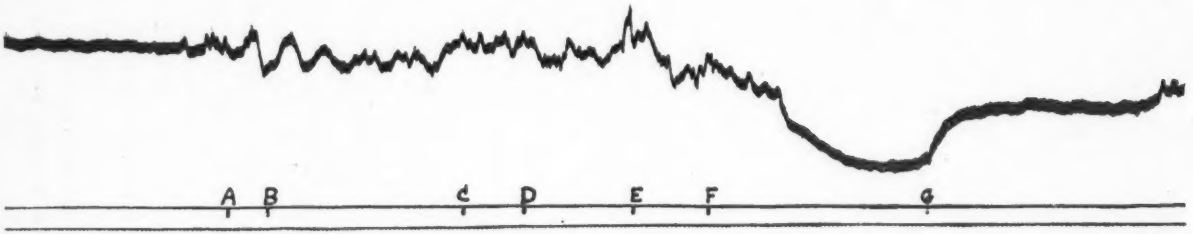

Fig. 1. Cat. Ether anaesthesia. A and B = clamping of left and right adrenal veins. C, D = ligating of collateral circulations (clamps on veins having been removed between B and C). E, F = clamping of left and right adrenal veins. G = release of clamps.

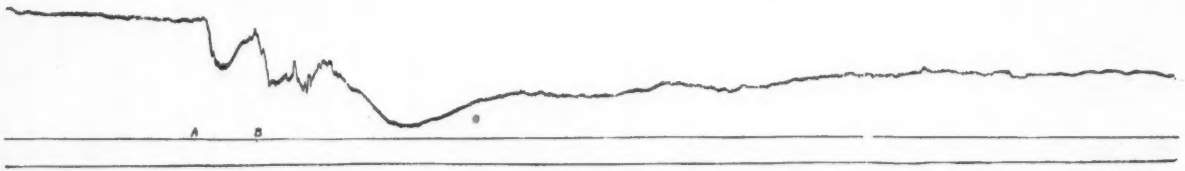

Fig. 2. Cat. Decerebrate. Fall of blood pressure following ligature of the adrenal veins (A, B), the collateral circulation having been previously ligatured. Note the gradual recovery process which reached completion in 30 minutes.

onstrated later, the presence of some anaesthetics is liable to introduce a fallacy due to a masking effect.

The methods employed in this long series of experiments are briefly as follows: The usual blood pressure record from the carotid artery was taken, and nothing done until the blood pressure maintained a constant level for at least a period of twenty minutes. The skin incision was then made (the glands were usually removed via the abdominal route), and the effect upon the blood pressure noted. If any fall of a magnitude equivalent approximately to that which might be expected as a result of adrenalectomy occurred, the animal was discarded so far as the present work was concerned. Similar precautions were adopted after the peritoneal cavity was opened and the intestine handled.

Ligatures were then placed upon the adrenal veins (as in the older experiments) and the effect upon the blood pressure carefully observed. The usual result was a transient fall of blood pressure. Recovery was rapid and the blood pressure remained at its original level. (Fig. 1. A, B.) This confirms the experiments done by this method. We have noticed that if during this procedure undue manipulation takes place small rises of blood pressure occur, presumably due to expression of adrenaline from the gland. In other experiments instead of ligating the adrenal veins, the collateral circulation was cut off. This can be done by placing ligatures round the small vein or veins draining the adrenal vein during its course across the gland and which can easily be found, and by tying a circular ligature round the posterior part of the gland. This latter procedure is somewhat difficult and must be done with care so as to avoid damaging the post ganglionic fibres from the semi-lunar ganglia, and also to avoid kinking the adrenal vein.

No change of blood pressure occurred as a result of the procedure. (Fig. 1. C, D.)

The adrenal veins were then clamped and a marked though gradual fall of blood pressure invariably resulted. (Fig 1.) The fall was considerable, often attaining the proportion of 50 mm. Hg. A direct relationship seems to exist between the initial height of the blood pressure and the depth of the fall. The fall persisted for approximately twenty minutes and there then began a very slow recovery which continued until the original pressure was reached. (Fig. 2.) If, however, the clamps on the adrenal veins were removed prior to the return of the original pressure, a very much sharper recovery occurred; indeed, in many instances it was almost immediate. (Figs. 1, 3.)

Precisely similar results have been obtained by reversing the order of the operative procedures, that is, clamping the adrenal veins first and the collateral circulation afterwards.

Complete adrenalectomy exhibited the same phenomena—the fall of blood pressure and slow subsequent recovery. (Fig. 4.)

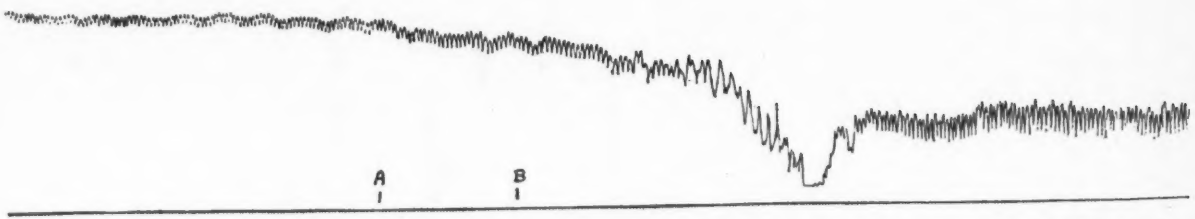

Fig. 4. Cat. Decerebrate. A = left adrenalectomy. B = right adrenalectomy. N.B.—There was a slow recovery comparable to that in Fig. 2 and which was completed in 20 minutes.

Fig. 5. Cat. Decerebrate. Both kidneys removed 20 minutes earlier; no change in blood pressure. At A, B complete adrenalectomy performed. No recovery from the fall of blood pressure occurred and the blood pressure remained constant at the lower level for one hour, after which the animal died from respiratory failure.

That these falls of blood pressure were not due to operative procedures was fully proved in several experiments in which various organs were removed before adrenalectomy. Removal of the kidneys for instance caused no variations in mean blood pressure, but subsequent adrenalectomy resulted in the fall of pressure above described. These falls of blood pressure cannot therefore be ascribed to vaso-motor reflexes caused by the abdominal manipulation [Vincent and Thompson (12)].

A very interesting variation of the usual result was obtained when any large portion of the splanchnic area was removed prior to the experiment. For example, when 3 feet of intestine was removed the recovery process was much delayed, and was never complete. The same effects were observed when the kidneys were removed; and if a sufficient area was extirpated there was a complete failure of the recovery process and the blood pressure remained constant at a much lower level than normal.. (Fig. 5.)

As already indicated, these results have been obtained in the decerebrate preparation and in the anaesthetised animal without exception. It must be pointed out, however, that the decerebrate preparation is not suitable for this experiment because so frequently respiratory failure develops [Vincent and Thompson (14), Bazett (2)] before the recovery of the

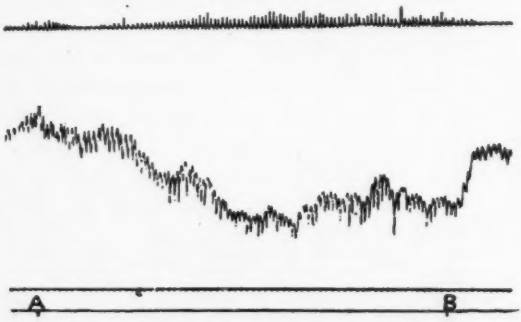

Fig. 3. Cat. Chloralose anaesthesia. Collateral circulation ligatured. Fall of blood pressure and recovery therefrom by clamping (A) and releasing clamps on (B) the adrenal veins.

blood pressure. The use of anaesthetics also possesses certain disadvantages; this especially refers to the volatile group. Variations in the depth of anaesthesia produces considerable alterations in blood pressure, thus entirely masking the result unless precautions are taken to insure a constant supply of anaesthetic, etc. For this reason chloralose and luminal sodium are most suitable.

DISCUSSION

Examination of the results shows that temporary depression of the blood pressure results from the elimination of the adrenal gland secretion from the circulatory system. The earlier workers failed to obtain this

result due to a leakage of adrenaline through collateral channels left open. Austmann and Halliday (1) using dogs under ether anaesthesia failed to obtain the depressor effect after adrenalectomy probably because of the difficulties associated with ether anaesthesia to which reference has already been made. It is significant to note, however, that these investigators make mention of exceptions in their series of negative results.

Our present investigations confirm much of Bazett's work (2). We have found, however, that the fall of blood pressure occurs much earlier than indicated by this work, and we believe that the recovery process is a most important factor. Apparently the vaso-motor mechanism, particularly of the splanchnic area, acts in a compensatory fashion after adrenalectomy so that in a short time the blood pressure has regained its normal level. Hence the failure to observe any depression of the blood pressure in survival animals after complete adrenalectomy. Therefore the adrenal glands should not be considered as essential to the maintenance of blood pressure as some earlier workers concluded, but should be described as a normally functioning accessory-mechanism the removal of which causes a transient fall of pressure. It may be noted here that we have frequently observed a marked slowing of the heart rate after adrenalectomy. The normal rate slowly returns during the recovery process. That the recovery process is not wholly due to the acceleration in heart rate is indicated by the fact that the recovery process is not completed after excision of a portion of intestine (vide supra).

Further, we believe that these facts adequately explain the low blood pressure in Addison's disease. Due to disease of the adrenal glands, there is lack of adrenaline and the consequent fall of blood pressure cannot be compensated because of the fibro-caseous involvement of the abdominal ganglia. Hence a persistently low blood pressure.

SUMMARY

Experiments have been performed upon anaesthetised and decerebrate cats demonstrating a fall of blood pressure when adrenaline is prevented from reaching the general circulation from the adrenal glands.

In order to obtain such a result it is essential that the collateral circulation should be tied as well as the adrenal veins.

The fall is not permanent, and the slow recovery is probably dependent upon vaso-motor control of the splanchnic area.

BIBLIOGRAPHY

1. Austmann, Halliday and Vincent: Trans. Roy. Soc. Canada, Sect. IV, 123. 1917.
2. Bazett, H. C.: J. Physiol. **53**: 320. 1920.
3. Cannon, W. B.: Am. J. Physiol. **33**: 356. 1914.
4. Cramer, W.: Fever, heat regulation, climate, and thyroid-adrenal apparatus, London. 1928.
5. Cow, D.: J. Physiol. **48**: 443. 1914.
6. Hoskins, R. G. and C. W. McClure: Am. J. Physiol. **30**: 192. 1912.
7. Moore and Purinton: Arch. f. de ges. Physiol. **71**: 483. 1900.
8. Stewart, G. N. and J. M. Rogoff: Endocrin. **1**: 150. 1917.
9. Strehl, H. and O. Weiss: Arch. f. d. ges. Physiol. **86**: 107. 1901.

10. Thompson, J. H.: J. Physiol. **65**: 441. 1928.
11. Vincent, S.: Brit. Assoc. Report of Ductless Glands Committee. 1912.
12. Vincent, S. and J. H. Thompson: J. Physiol. **65**: 327. 1928.
13. Vincent, S. and J. H. Thompson: J. Physiol. **65**: 449. 1928.
14. Vincent, S. and J. H. Thompson: Endokrinol. **5**: 335. 1929.
15. Vincent, S. and S. Wright: Quart. J. Exper. Physiol. **14**: 285. 1924
16. Young and Lehmann: Proc. Physiol. Soc. **37**: 54. 1908.

ESTROGENIC SUBSTANCES: I. APPARATUS AND METHODS FOR PREPARATION OF STABLE EXTRACTS FROM NATURAL SOURCES

JAMES C. JANNEY, M.D., F.A.C.S., AND BURNHAM S. WALKER, Ph.D.
From the Evans Memorial and Boston University School of Medicine
BOSTON, MASS.

The introduction by Allen and Doisy (1) of the vaginal spread method of testing for the ovarian hormone has led to an enormous number of investigations involving the induction of estrus in castrated female animals. The literature on this subject has been assembled and correlated in the valuable monograph of Frank (2), who gives a bibliography of 491 titles covering the literature up to 1929.

Since the publication of Frank's monograph, the crystallization of the ovarian hormone has been reported by Doisy, Veler and Thayer (3) and by Butenandt (4). These discoveries, if substantiated, will constitute the second major advance in the study of the chemical mechanism of estrus, and more broadly, of the chemistry of reproduction in the female.

Substances capable of inducing estrus in castrated female animals apparently have a very wide distribution in nature. Estrogenic material has been obtained from follicular fluid (5), corpora lutea (6), placenta (7), blood (8), urine (9), amniotic fluid (10), liver (11), bile (12), milk (10), testis (13), feces (14), bird's eggs (13), and many plant materials, including yeast (15), grains (13), garden vegetables (16) and flowers (17). Whether or not active materials from different sources are chemically identical is still unknown.

This paper deals with methods for the convenient preparation of actively estrogenic extracts from some of the natural sources. No special claim for originality in principle can be made for any of these procedures. Our purpose is to present *in detail* methods which have been found to combine adequate yield with convenience of manipulation. The majority of published work has emphasized the chemical properties and physiological effects of the extracts, giving only scanty description of the initial stages of preparation.

EXTRACTION FROM URINE

Urine from women in the last three months of pregnancy was obtained from a maternity home. Collections were made in 15 liter carboys, about 200 cc. of chloroform being added to each carboy before the collections were made, to serve as a preservative, and to add to the chloroform used later as an extraction medium.

We selected chloroform as the solvent from the first, on account of its availability, non-inflammability and freedom from such harmful oxidizing substances as may be present in ether (18).

In the extraction, we avoided the usual procedure of previous concentration. The evaporation of large volumes of urine in open dishes is at best an unpleasant process; vacuum evaporation would involve apparatus beyond our means or those of the average laboratory, unless carried out at a very slow rate. Preliminary experiments with separatory funnel extractions led us to believe that the partition coefficient of the active material between chloroform and water was sufficiently high to permit direct extraction without previous concentration.

The extraction apparatus, which is of the impluviation type, is shown in Fig. 1.*

An all-glass apparatus is imperative. Rubber stoppers are entirely out of the question, since they are rapidly dissolved by chloroform. Cork stoppers are longer-lived but yield in the extract noticeable quantities of a crystalline material, M.P. 236° C., free from ash, nitrogen, phosphorus or sulfur. This material can be easily obtained by refluxing cork with chloroform and recrystallizing the residue from the evaporation of the chloroform with ethyl acetate.

Extraction is carried out as follows: the urine container, an ordinary 5-gallon glass carboy, is charged with 15 liters of urine and one liter of chloroform. The flask of the extraction apparatus is filled with chloroform (before the carboy is put in place) by dipping the long tube in chloroform and applying suction at the condenser outlet, with the stopcock closed. When the flask is nearly full, the stopcock is opened and the tube removed from the chloroform. The opening of the stopcock prevents siphoning out of the chloroform. After the tube has been inserted into the carboy, the siphon can be started by applying suction at the stopcock. An asbestos board should be placed between the carboy and the electric plate, as shown in the diagram. From then on all that is necessary is to supply current to the electric plate and water to the condenser, to keep the extractor running as long as may be desired. The only possibility of anything going wrong is the occasional leakage of air around the stopcock, resulting in the breaking of the fluid column in the siphon. This has happened a few times, but we have not greased the stopcock lest we contaminate the extract.

Our time of extraction has been uniformly 16 hours (two working days). We do not recommend leaving the extractors entirely unattended over night, on account of the possibility of failure of the siphon by the (very occasional) leakage of the stopcock.

To remove most of the chloroform extract it is only necessary to remove the extractor from the urine carboy and allow the extract to siphon out. We usually let the small residual chloroform in the bottom of the flask remain and proceed with the next extraction. If it is desired to remove all the extract, it can be poured out through the condenser. The

*We are indebted to Mr. F. S. Macalaster, who built the apparatus for us, for certain modifications increasing the compactness and mechanical strength of the extractor, and to Mr. Albert Copans, for making the drawings.

apparatus may be cleaned by filling the flask in the usual manner with 10 per cent alkali, heating to boiling, and then flushing out thoroughly with a stream of water led in through the long tube.

The excess chloroform can be distilled off the extract in any ordinary distillation apparatus, using a steam bath as the source of heat. If stoppers are used they should be protected with tinfoil. A compact all-glass distillation apparatus with a vertical spiral condenser is to be recommended.

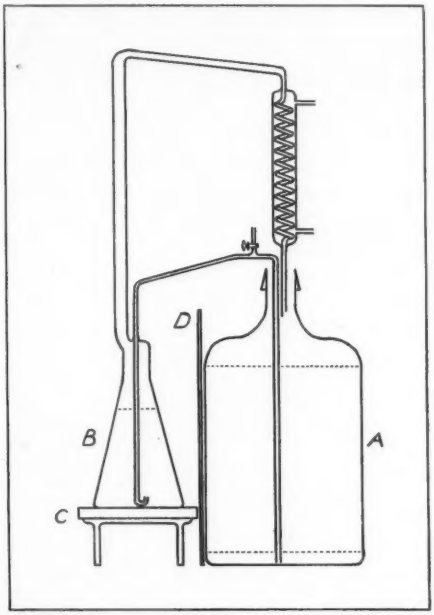

Fig. 1. Extraction apparatus for urine. A, Urine container (5-gallon glass carboy). B, Chloroform flask. C, Electric plate. D, Asbestos board.

The product should be kept in chloroform solution in dark glass bottles with glass stoppers. Under such conditions, as we will show later, extracts do not lose potency in a year at room temperature.

EXTRACTS FROM TISSUES

It seemed desirable, if possible, to apply a similar process of continuous extraction to tissues. Most investigators have either desiccated the tissues or used solvents miscible with water. In our experience, drying of tissues either in air or in vacuum (using apparatus available in the laboratory) was uniformly accompanied by a certain amount of decomposition, resulting in loss of potency and introduction of toxic or otherwise objectionable materials into the extract. The use of a water-miscible solvent, such as alcohol, resulted in the extraction of a much larger amount of inert material, most of which was difficult to separate.

Extraction by impluviation is not applicable to solid material since the solvent will tend to follow definite paths through the material, and portions will remain untouched. With desiccated tissue, simple standing or heating with the solvent is quite satisfactory. Our purpose, then, was to combine the desiccating and extracting processes, allowing the gradual removal of water while the material was in contact with the solvent.

With this in view, an all-glass apparatus was devised, involving the automatic separator of Hultman, Davis and Clarke (19). This apparatus is shown in Fig. 2. The fresh, wet tissue is heated in the flask with chloroform. Chloroform and water distill off together in a definite proportion which depends upon their relative vapor pressures at the temperature of

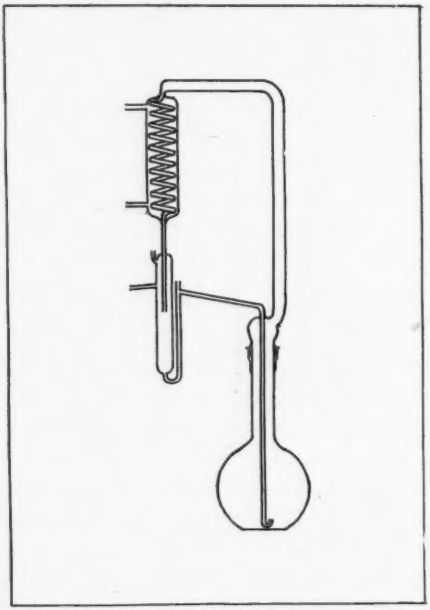

Fig. 2. Extraction apparatus for tissue.

distillation. The vapors condense and pass into the automatic separator where the heavier chloroform sinks to the bottom and is returned to the flask. The water rises and escapes from the side tube.

This process, although rather slow, requires no attention whatever beyond the supply of heat to the flask and water to the condenser. At the medium heat of the electric plate used, about 400 grams of water can be removed from a sample of tissue in eight hours. By the time the water is removed, there is uniform distribution of chloroform-soluble material and the majority of it may be removed by a simple filtration. If complete extraction is desired, a brief repetition of the refluxing with fresh chloroform will accomplish this purpose.

POTENCY AND STABILITY OF CHLOROFORM EXTRACTS

The crude extract can be tested for its estrogenic power by simply evaporating the chloroform completely (small traces are toxic) from a small aliquot, taking up the residue in 2 cc. oil sesame and injecting the oil solution into a castrated female mouse in three portions, three hours apart. The technique of castration, preliminary control smears, injection, reading of test smears and interpretation is that used by Janney (20). It should be noted that such procedures vary a great deal with different workers and that in comparing results from different laboratories, variations in technique and interpretation must be considered.

We find that amounts of crude extract equivalent to one cc. of original urine are usually sufficient to cause estrus. This figure does not represent the actual concentration of estrogenic material in the urine, since with further purification and the use of an aqueous medium for injection, amounts equivalent to less than one cc. of original urine will produce estrus.

That chloroform extracts suffer no great loss of potency over long periods of time is shown by the following experiment. A portion of a chloroform extract of urine was diluted so that one cc. was equivalent to one cc. of the original urine. This extract was placed in a brown bottle with glass stopper and kept in a closet in the laboratory. One year later, one cc. portions were evaporated, dissolved in oil of sesame and injected into six test mice, all of which gave full positive reactions. The extract had in the meantime deposited a dark, adherent sediment which proved inactive.

POTENCY AND STABILITY OF AQUEOUS PREPARATIONS

The injection of oil solutions into mice has certain disadvantages; it sometimes remains in the site of injection for many days, occasionally causing extensive sores. We have in all cases preferred injection in an aqueous medium whenever it was feasible. Isotonic sodium chloride solution is the ideal medium for injection. We have observed with surprise that none of the numerous investigators have mentioned this very obvious expedient. Many speak of water suspensions; in our experience water injections always cause sloughing at the site of injection, as well as obvious signs of discomfort on the part of the mouse during injection. Saline suspensions cause the mouse no apparent pain and no bad after-effects.

By using the method of Zondek (21) with the single modification of using saline instead of water as the final vehicle, it is possible to obtain from the crude chloroform extract a preparation with a greater potency per unit of original urine than the crude extract itself. This may indicate either an inhibiting effect of impurities, or more complete absorption from the aqueous medium. A preparation made according to Zondek (saponification of residue from chloroform extract, extraction from aqueous alkaline suspension with ether, suspension of residue from ether evapora-

tion in saline, dilution and injection) with the use of saline as the injection medium, gave the following results:

TABLE I

Urine equivalent of dose	Number of mice	Number positive	Number negative
10 cc.	2	2	0
5	2	2	0
1	2	2	0
0.5	2	2	0
0.1	2	1	1

The preparations by Zondek's method appear to lack stability. Whether kept in the cold or at room temperature, they show loss in potency after a week. This same extract, one week later, was negative in doses equivalent to 2 cc. urine, and two weeks later, negative in doses equivalent to 5 cc.

A more stable aqueous preparation was made by further treatment of the product of the Zondek procedure. A chloroform extract of 420 liters of urine was evaporated just to dryness. The residue was boiled with concentrated sodium hydroxide, cooled and extracted with ether. The ether extract was evaporated to dryness and the residue boiled with 2 per cent acetic acid (420 cc.) and filtered. The filtrate was found to be active, but most of the material remained undissolved. This insoluble residue was dissolved in 95 per cent alcohol, boiled with bone-black and filtered. From the alcoholic solution crystals separated, which were found to be identical with the unidentified solid alcohol described by Marrian (22). In agreement with Marrian, we found that these crystals had no estrogenic activity. The (alcoholic) mother liquor from this crystallization was evaporated to dryness, taken up in chloroform, filtered and the chloroform evaporated off. The residue was extracted with boiling water, which gave a turbid suspension; this was diluted to 250 cc. A number of mouse tests were carried out on this extract, showing that it contained about one-eightieth of the total estrogenic material of the original urine (assuming one mouse unit per cc.). This extract was stable for over four months, as shown in Table II. No special precautions were taken for its preservation, it being kept in an ordinary glass-stoppered flask in diffuse daylight and at room temperature. All doses were made up to 2 cc. with saline.

TABLE II

EXTRACT PREPARED OCTOBER 2, 1929.

Date	Dose (cc. extract)	Number of mice	Number positive	Number negative
Nov. 6	.25	5	5	0
	.13	4	4	0
	.06	4	4	0
Nov. 13	.10	6	6	0
	.01	6	0	6
Nov. 20	.05	2	2	0
Dec. 4	.05	6	5	1
Mar. 24	.05	5	3	2
Apr. 9	.05	9	7	2

Stable aqueous extracts can also be prepared by other slightly different procedures. For the final extraction with boiling water can be substituted the addition, drop by drop, of an ether solution of the active material to saline heated well above the boiling point of ether. The keeping qualities of such a preparation are shown in Table III.

TABLE III

EXTRACT PREPARED DECEMBER 10, 1929.

Date	Dose (cc. extract)	Number of mice	Number positive	Number negative
Dec. 10	2	5	5	0
Dec. 18	1	5	5	0
Dec. 18	0.5	5	4	1
Mer. 5	2	2	2	0
Mar. 12	1	2	1	1
Mar. 12	0.5	2	2	0

TISSUE EXTRACTS

The tissue extractor has not been used for as long a time as the urine apparatus, but has given very satisfactory results. Our type procedure is as follows: the tissue is ground in a meat chopper and introduced into the flask of the apparatus. A volume of chloroform is added at least as great as that of the tissue. The condenser is then attached and heating continued until water ceases to be given off (this requires from 16 to 32 hours with a placenta). The chloroform and water usually form an emulsion in the flask, which clears as the water is eliminated.

When water is no longer given off, extraction is considered complete and the chloroform is filtered from the residual solid. The extract is evaporated to small volume and an excess of sodium hydroxide solution added. The mixture is allowed to saponify half an hour on the steam bath, is then cooled and extracted with ether in a separatory funnel. If an emulsion forms it can be broken by the addition of solid sodium sulfate.

The ether extract is evaporated, taken up in saline and injected without filtering. The amount of extra material is much greater in the tissue extracts than in the urine preparations and the suspensions are quite turbid.

Extracts have been made from placenta and from liver following this procedure; in both cases the minimum effective mouse dose is the equivalent of 5 grams wet tissue. The finding of estrogenic material in the liver is in agreement with the results of Schröder and Goerbig (23), who found that injection of liver lipoids caused growth of the uterus in immature rabbits, and with Dingemanse and Laqueur (11), who found estrogenic material in liver and bile. The bile as a source of estrogenic material has also been studied by Gsell-Busse (12).

SUMMARY

1. Apparatus for the convenient extraction of estrogenic material in large quantity from urine and tissue is described.

2. Preparation of crude chloroform extracts (stable for at least a year) and of more purified aqueous suspensions (stable for at least four months) is outlined.

3. Isotonic salt solution is recommended as the most satisfactory injection medium.

BIBLIOGRAPHY

1. Allen, E. and E. A. Doisy: J. A. M. A. **81**: 819. 1923.
2. Frank, R. T.: "The Female Sex Hormone." Thomas, Springfield. 1929.
3. Doisy, E. A., C. D. Veler and S. Thayer: Proc. XIII Physiological Congress, Page 67. Am. J. Physiol. **90**: 329. 1929.
4. Butenandt, A.: Naturwissenschaften, **17**: 879. 1929.
5. Allen, E., J. P. Pratt and E. A. Doisy: J. A. M. A. **85**: 399. 1925.
6. Allen, E., J. P. Pratt, Q. U. Newell and L. J. Bland: Am. J. Physiol. **92**: 127. 1930.
7. Allan, H., F. Dickens, E. C. Dodds and F. O. Howitt: Biochem. J. **22**: 1526. 1928.
8. Loewe, S.: Klin. Wchnschr. **4**: 1407. 1925.
9. Loewe, S. and F. Lange: Klin. Wchnschr. **5**: 1038. 1926.
10. Brouha, L. and H. Simonnet: Compt. rend. Soc. de biol. **97**: 459. 1927.
11. Dingemanse, E. and E. Laqueur: Arch. néerl. de physiol. **14**: 271. 1929.
12. Gsell-Busse, M. A.: Arch. f. d. ges. Physiol. **219**: 678. 1928. Also Arch. f. exper. Path. u. Pharmakol. **139**: 328. 1929.
13. Fellner, O. O.: Klin. Wchnschr. **4**: 1651. 1925.
14. Dohrn, M. and W. Faure: Klin. Wchnschr. **7**: 943. 1928.
15. Glimm, E. and F. Wadehn: Biochem. Ztschr. **197**: 442. 1928.
16. Dohrn, M., W. Faure, H. Poll and W. Blotevogel: Med. Klin. **22**: 1417. 1926.
17. Loewe, S., F. Lange and E. Spohr: Biochem. Ztschr. **180**: 1. 1927.
18. Thayer, S., C. N. Jordan and E. A. Doisy: J. Biol. Chem. **79**: 53. 1928.
19. Hultman, I. N., A. W. Davis and H. T. Clarke: J. Am. Chem. Soc. **43**: 366. 1921.
20. Janney, J. C.: Arch. Surg. **18**: 1241. 1928. Also Am. J. Obst. & Gynec. **18**: 807. 1929.
21. Zondek, B.: Klin. Wchnschr. **7**: 485. 1928.
22. Marrian, G. F.: Biochem. J. **23**: 1090. 1929.
23. Schröder, R. and F. Goerbig: Ztschr. f. Geburtsh. u. Gynäk. **83**: 764. 1921.

A METABOLIC STUDY OF DESICCATED SUPRARENAL MEDICATION IN MAN

R. G. HOSKINS AND F. H. SLEEPER
Worcester State Hospital
WORCESTER, MASSACHUSETTS

Desiccated suprarenal substance has been in use as a therapeutic agent for many years. It is a standard article of commerce in the pharmaceutical trade. There are in the literature many nebulous claims of benefit following its use, but of reports of clean-cut, controlled investigation in human subjects there is a dearth.

For the past three years we have been engaged in a diagnostic-therapeutic study of the subject of dementia praecox. Among some 130 patients subjected to somewhat elaborate diagnostic study, more than half have shown functional deviations from normality that point toward endocrine deficiency. One common picture presented in this disorder is reduction of body temperature, blood pressure, and basal metabolic rate; secondary anemia; and reduction of bodily vigor. This picture is suggestive of adrenal deficiency. In numerous instances suprarenal substance has been administered alone or in combination with other medicaments. The general conditions under which the work was carried out have been previously reported (1).

Among the series of cases so treated, nine have been selected in which satisfactory test conditions obtained. The suprarenal substance was administered by mouth in dosages varying from 18 to 90 grains daily, and for periods of 54 to 108 days. In eight cases the suprarenal substance was used alone; in one, it was superimposed upon a preceding course of thyroid treatment. The subjects were all males, ranging in age from 23 to 40 years.

Before the medication was begun, determinations were made, among other things, of urine volume; total urinary nitrogen; basal metabolic rate; blood pressure; pulse; temperature; erythrocyte count; leucocyte count; percentage of various types of the white cells; non-protein nitrogen; uric acid and sugar in the blood; galactose tolerance; body weight; and "lung volume" as indicated by spirometer measurements. Standard methods of making the various tests were employed, as previously reported (1). In this series, "Suprarenal Emplets" of Parke-Davis & Co. and a special preparation of adrenal cortex made by Reed & Carnrick were administered.*

An inspection of the accompanying table shows that the results have been essentially negative throughout. Likewise no significant mental

*It is a pleasure to record our obligation to these firms, as well as to Armour & Co., for generous supplies of suprarenal material.

LABORATORY FINDINGS IN 9 CASES OF DEMENTIA PRAECOX BEFORE AND AFTER TREATMENT WITH DESICCATED SUPRARENAL SUBSTANCE

Patient	C. A.	J. D.	H. K.	A. McF.	D. S.	G. S.	J. T. S.	A. T.	J. T.	Avgs.
Age	31	25	29	36	23	30	40	35	33	31.3
Years in hospital	3	9	10	3	1	5	2	6	6	5.0
Preparation used	R & C	R & C and P & D	P & D	P & D	R & C	*R&C and P & D	R & C	R & C and P & D	R & C	
Dosage in grains	18	75 42	60	40	30	38	20	90 42	48	45.7
Period of treatment, days	82	25 34	89	36	97	77	54	30 58	108	61
Urine Amount										
Control period	1750	4640		1540	1300	1117	3630		655	2090
Experimental period	1854	4620		2660	1480	1140	756		1185	1956
Urine Nitrogen										
Control period	15.7	13.1			12.2	9.0	11.4		6.8	11.4
Experimental period	10.7	14.8			11.5	7.3	9.0		9.0	10.4
Basal Metabolism										
Control period	94 ?	82	72	98	88	70	90	90	96	87
Experimental period	98 ?	89	71	95	86	62	79	86	85	83
Blood Pressure										
Control period	102/58	76/40	96/40	112/35	128/55	100/60	98/46	100/42	96/52	101/47
Experimental period	108/60	98/45	96/30	113/43	106/52	88/54	100/40	106/36	94/56	101/46
Pulse Rate										
Control period	79	47	49	61	56	50	51	49	54	55
Experimental period	83	61	48	70	47	52	49	53	52	58
Rectal Temperature										
Control period	97.3	97.4	97.0	98.4	98.0	97.8	97.3	99.2	97.6	97.8
Experimental period	98.4	98.8	98.8	98.0	97.6	99.0	97.8	99.4	97.2	98.3
Erythrocytes x 1000										
Control period	6,330	5,140		5,200	5,500	5,360	4,390	4,660	4,780	5,172
Experimental period	4,720	4,965		5,680	4,260	5,010	5,360	5,180	4,710	4,998
Leucocytes x 100										
Control period	58	84.5		71	110.5	64.5	80	80.5	77	75.9
Experimental period	76	88		82	99.5	56.5	76	106	94	81.5
Lymphocytes										
Control period	24	43.5		27.5	46.5	34.5	20.5	20	34	31.4
Experimental period	32.5	42		28	49.5	34	42.5	21	44.5	36.6
Eosinophiles										
Control period	3	7.5		2	1.5	1	.5	2.5	3	2.6
Experimental period	2.5	4.5		1.5	2	0	.5	1.5	6.5	2.1
Blood N. P. N.										
Control period	34	29		32	34	30	28	32	33	31.1
Experimental period	25	29		30	30	29	28	30	30	29.1
Blood Uric Acid										
Control period	3	1.6		2.8	2.9	3.4	1.8	3.5	2.1	2.8
Experimental period	2.6	3.3		3.3	3.3	3.0	3.0	3.5	1.9	3.0
Blood Sugar										
Control period	95	110		97	91	98	90	83	95	107
Experimental period	115	63		91	100	108	87	80	112	94
Galactose Tolerance										
Control period	20	20	30	10	20	20		20	20	20
Experimental period	20	20	20	20	20	10		20	—10	16
Weight										
Control period	60.0	66.4	50.2	61.4	72.2	44.0	56.4	56.0	54.1	58.0
Experimental period	64.6	65.6	51.6	62.0	74.4	49.0	65.0	59.4	51.0	60.4
Vital Capacity—% of Normal										
Control period	96	100		80	85	86	93	99	83	90
Experimental period	100	108		80	80	88	80	94	93	90

*P-D & Co. Suprarenal Emplets substituted for two periods of 5 and 6 days each.

changes have been detected. Such deviations as occur in the medication periods as compared with the control periods are within the limits of experimental error and, in general, are not consistent in direction from one patient to another.

Primary interest attaches to the blood pressure and the basal metabolic rate. In three cases, the systolic level was higher after medication, in two cases lower, and in four cases essentially unchanged. The averages happen to be exactly equal. The basal rate was increased in two, lower in five, and essentially unchanged in two cases, and the average was slightly decreased. There is a suggestion of partial normalizing of the body temperature. The average erythrocyte count was decreased, though in three instances it was increased. The data, as a whole, fail to indicate any significant efficacy of the preparations used.

While it must be recognized that nine cases are too few to justify absolute conclusions, nevertheless under the conditions of these experiments any efficacy of the substance sufficient to be of practical clinical significance could hardly have failed of indication. At any rate, these negative results serve further to cast the burden of proof on those who regard the oral administration of desiccated suprarenal substance to adults as other than psychotherapy.

That such material may exercise some influence on developmental processes in young organisms is not, in this connection, a pertinent fact.

SUMMARY

A controlled study of various metabolic processes and morphological features in nine adult male schizophrenic human subjects has failed to indicate that desiccated suprarenal substance administered in large doses by mouth is of any significant therapeutic value.

(1) Hoskins, R. G., and F. H. Sleeper: This Journal, 13: 245; 13: 459. 1929.

Book Reviews

EL SISTEMA NERVIOSO AUTONOMO EN LA REGULACION DE LA GLUCEMIA. J. Puche Alvarez. Rev. méd. de Barcelona, **8**: 344. 1927.

The author reports a series of some 50 experiments on the effects of various influences on the blood sugar level. This level was found to be lowered by vagus stimulation, asphyxia after splanchnic and hepatic nerve block, choline (in man and rabbits but not in dogs) and eserine. Pilocarpine caused an increase in the blood sugar in normal animals but augmented the hypoglycemia of adrenal deficiency. Atropine had no demonstrable effect. It is concluded that the autonomic nervous system has an indubitable regulating influence on carbohydrate metabolism through its influence on the endocrine glands especially concerned therewith.

THE FEMALE SEX HORMONE. Robert T. Frank. 1929. Charles C. Thomas, Springfield, Illinois. Pp. 321.

The author has been personally active as an investigator throughout the significant period of development of our knowledge of the subject. He writes, therefore, with an excellent historical perspective. The first section of the work comprises a detailed treatment of the biology, pharmacology and chemistry of the subject. The embryology and anatomy are clearly presented and then a chapter is devoted to physiological experiments, such as extirpation and transplantation of the ovary. The chapter on the experimental results of injecting extracts is especially good. Without detailing further topics treated, suffice it to say that the student will find every modern phase of the subject succinctly treated. The more crucial experiments have mostly been performed originally or have been repeated by the author and his colleagues, hence he shows a firm touch in his critical estimates of the data. The remainder of the book is devoted to clinical considerations. It, too, is good, but is less fresh, since much of the material is more or less commonplace gynecology.

The work is clearly written throughout and is well printed. The illustrations are abundant and generally clear. A well selected bibliography closes each section of the book.

The book as a whole accomplishes admirably what is, one assumes, its fundamental purpose, of putting the reader in close touch with the significant current knowledge throughout the field. It is timely and adequate.

MANUEL DE LAS ENFERMEDADES DEL TIROIDES. G. Marañon. 1929. Manuel Marin, Barcelona. Pp. 211.

Marañon has added another to the list of several recent excellent books on thyroid disease. He has followed what has come to be the conventional plan in writing such books—giving chapters to "physiology," "anatomy," etc., then to each of the varieties of thyroid disorder. The book, although exhibiting the author's catholicity of knowledge of the world's literature, is of particular significance in its bringing together the outstanding material written in the Spanish language. The work is well printed and the illustrations plentiful and interesting. They are largely from the author's own experience.

Abstract Department

Experimental epithelioma in white mice as influenced by adrenal grafts from rabbits treated with the same tumor (Modifications évolutives de l'épithélioma experimental de la Souris blanche par greffes de surrénales provenant de Lapins préparés avec ce même épithélioma). Arloing, F., A. Josserand and J. Charachon, Compt. rend. Soc de biol. **100:** 1035. 1929.

Rabbits were given subcutaneous injections of crushed tumor, a total of 1.9 grams in three doses in nine days. A week later the adrenals were transplanted into tumor-bearing mice. They had an inhibitory effect on the tumor growth not possessed by adrenals from untreated rabbits. This lasted about a week. The adrenals of the injected rabbits showed no gross or microscopic changes a week after the injections stopped. Two weeks after they were doubled in size, the cortex swollen and the medulla degenerated. At this time their inhibitory influence on tumor growth was unreliable. Later, it seemed actually altered, so that the adrenal grafts favored the growth of the epithelioma.—J. C. D.

Relations between changes in the adrenal cortex and alterations in experimental cancer in white mice (Relations entre les modifications de la cortico-surrénale et l'évolution du cancer expérimental de la Souris blanche). Arloing, F., A. Josserand and J. Charachon, Compt. rend. Soc. de biol. **101:** 646. 1929.

These authors agree with Sokoloff that there is increased activity and later degeneration of the cortex and that in the first phase there is an action of the gland inimical to the tumor.—J. C. D.

Lecithin and lecithin ferment in arterial blood and that of the adrenal (Lécithine et lécithinases dans le sang artériel et dans le sang surrénal). Bianco, J., Compt. rend. Soc. de biol. **102:** 463. 1929.

Observations on the lecithin content and lecithin splitting power of arterial, venous and adrenal blood are given. The animal used is not named. The adrenal pours lecithin into the blood stream and also supplies to it a lecithin splitting ferment.—J. C. D.

Adrenaline vasodilatation. Dunlap, H. H., J. Physiol. **67:** 349. 1929.

Ether diminishes both the vasoconstriction and cardiac effect of adrenaline. The fall of blood pressure after small doses is due to vasodilatation in skeletal muscles, and diminution of active visceral vasoconstriction.—C. I. R.

Methods for testing for the presence of adrenal cortex hormone. Flory, E., A. Szent-Gyorgyi and M. E. Flory, J. Physiol. **67:** 343. 1929.

Study of muscular fatigue in cats deprived of adrenal cortex convinced the authors that the method is not reliable for detection of the presence of the contex hormone.—C. I. R.

Histophysiology of the adrenal in experimental arterial hypertension (Histophysiologie de la surrénale pendant l'hypertension artérielle expérimentale). Goormaghtigh, N. and L. Elaut, Compt. rend. Soc. de biol. **101:** 501. 1929.

Denervation of the carotid sinus and root of the aorta in rabbits produces hypertension. In such animals, the adrenal medulla shows in the first day a rapid exhaustion of adrenin followed over a period of months by an accumulation in excess of normal. Hypertrophy is not noticeable. The cortex shows a rapid reduction in cholesterin the first day, and then a steady accumulation together with a true hypertrophy of the cortex and numerous mitotic figures in the glomerulosa. This suggests an increase in blood cholesterol. Clinically such cases of hypertension are seen with enlarged adrenals. These results suggest that the adrenal enlargement results from the hypertension and not vice-versa.—J. C. D.

Arterial blood pressure and blood flow in skeletal muscles as influenced by epinephrine. Gruber, C. A., Proc. Soc. Exper. Biol. & Med. **26**: 472. 1929.

In unanaesthetized cats small doses of epinephrine invariably caused an increase in the rate of blood flow in skeletal muscles irrespective of the change in blood pressure. Large doses of epinephrine rapidly injected intravenously caused an increase in blood pressure accompanied by a decrease in rate of blood flow in skeletal muscle. Following the rise the blood pressure fell below the normal level and simultaneously with it a marked increase in the rate of blood flow through the muscles was observed.—M. O. L.

Effect of yohimbine on adrenin's influence on blood sugar (Action de la yohimbine sur les effets de l'adrénaline a l'égard du sucre du sang).

Reinforcement of the hypoglycemic effects of insulin by yohimbine (Renforcement des effets de l'insuline sur le sucre du sang au moyen de la yohimbine). Hanson, S., Compt, rend. Soc. de biol. **101**: 603. 1929.

Yohimbine paralyzes the sympathetic motor nerve endings. As a result, when injected into rabbits, it abolishes the hyperglycemia produced by adrenin and reinforces markedly the hypoglycemia resulting from insuline.—J. C. D.

Effect of adrenalin and cholic acid on creatinin excretion (Über den Einfluss des Adrenalins und der Cholsäure auf die Kreatininausscheidung). Kaziro, K. and A. Taku, J. Biochem. **11**: 203. 1929.

In male rabbits, the hourly and daily excretion of creatinin is increased by subcutaneous administration of adrenalin, and decreased by subcutaneous administration of sodium cholate.—B. S. Walker.

The function of the interrenals in Torpedo (Die Funktion des Interrenalgewebes bei Torpedo). Kisch, B., Endokrinol. **1**: 31. 1928.

The interrenals of the Torpedo, which are analogous to the cortex of the adrenal gland of higher animals, apparently contain the so-called adrenal hormone, since removal causes muscular weakness followed by early death due to respiratory failure. There are also pigmentation changes. Similar results are not obtained by operation without the removal of the gland. Addition of interrenal extract relieves the symptoms.—B. C.

Thyroid function and the pressor action of adrenalin (Schilddrüsenfunktion und Blutdruckwirkung des Adrenalins). König, W., Arch. f. exper. Path. u. Pharmacol. **134**: 36, 1928.

The pressor responses to injections of adrenalin in various concentrations in normal and thyroidectomized dogs were studied following the subcutaneous administration of thyroxin. It was found that thyroxin administration did not increase the sensitivity to adrenalin in normal animals. Even a longer treatment with thyroxin had no uniform effect on the responses to adrenalin in normal dogs. In thyroidectomized dogs the effectiveness of adrenalin was definitely diminished. The responses could be restored to the normal level by administration of thyroxin. It was concluded that the failure of the thyroid function lessened the reaction toward the sympathicomimetic pressor substance, adrenalin. From the failure of effect of thyroxin administration in certain experiments and from the certain results of thyroxin administration after thyroidectomy it is probably indicated that the thyroxin effect is concerned with the metabolism and not directly with action on any organs.—L. C. Wyman.

Responses of the kidney and spleen to subcutaneously injected epinephrin. Koppanyi and M. S. Dooley, Proc. Soc. Exper. Biol. & Med. **26**: 443. 1929.

In anesthetized dogs massage of areas injected with epinephrin may produce marked localized vasoconstrictor effects, even when the general blood pressure remains unaffected. Kidney and spleen volume changes are more easily elicited with small amounts of epinephrin than a change in general systolic blood pressure.—M. O. L.

The effect of repeated injections of insulin on the suprarenals of rabbits (Der Einfluss chronischer Insulinzufuhr auf die Nebennieren beim Kaninchen). Langecker, H., Arch. f. exper. Path. u. Pharmacol. **134:** 155. 1928.

Experiments were carried out on growing male rabbits which received a series of injections of insulin, averaging about 30 in the course of one year. The absolute and relative weights of the suprarenal glands, as well as the "standard variation," were determined in both normal and experimental animals. Biological and colorimetrical assays of the adrenalin content were also made. It was concluded that the suprarenals of rabbits continuously treated with insulin were, on the average, heavier than those of normal rabbits. The difference was not great but was large enough in order to assume from a study of the standard variation that suprarenal hypertrophy occurred after insulin administration. The determination of the adrenalin content is of value only if estimated at least seven days after the last injection of insulin, since the gland loses its effective pressor substance which is only gradually made up. Despite the diminution of the biological, and according to some authors the morphological demonstrable adrenalin, the colorimetrically determined adrenalin content is unaltered. It can be assumed that the reducing constituent of the gland, which stands in some genetic relation to adrenalin, is in no way affected, and that the pressor substance is secreted under the influence of insulin administration. The suprarenal hypertrophy in the course of continuous insulin administration is due for the most part to enlargement of the cortex, but since the absolute adrenalin content is still greater than normal it is indicated that the medulla is also involved, though to a much less degree.—L. C. Wyman.

Adrenin content in three cases with adrenal tumor. The relation between the histology of the tumor and the patient's blood pressure (Dosage de l'adrénaline dans trois cas de tumeurs surrénales. Rapports avec la structure histologique de la tumeur et la tension artérielle du malade). Langeron, L., M. Paget and P. Lohéac, Compt. rend. Soc de biol. **100:** 873. 1929.

Two epitheliomas of the cortex and a sympathetic cell tumor were studied. The adrenin contents did not agree with the histology in one case and in another there was an increased blood pressure although no increase in adrenin was seen.—J. C. D.

The use of epinephrine as a diagnostic test for angina pectoris. Levine, S. A., A. C. Ernstene and B. M. Jacobson, Arch. Int. Med. **45:** 191. 1930.

Epinephrine was administered subcutaneously in doses of 1 cc. to three groups of persons; one group of 11 with angina pectoris, a second of 10 of the same average age but without angina, and a third of 10 normal young adults. In all but one patient with angina pectoris, typical pain resulted from the injection. In none of the control patients did this pain occur. Electrocardiographic studies showed that following the injection of epinephrine the T wave in the angina group increased slightly in amplitude, while in the other two groups it showed a tendency to decrease. The increase in blood pressure and pulse rate was somewhat greater in the anginal group than in the others. It is suggested that the production of anginal pain by the injection of epinephrine may serve as a diagnostic test for angina pectoris. The test would not be applicable when the diagnosis is certain but rather in doubtful cases or when there are other possible explanations for the symptoms, such as gallstones or disease of the stomach or the duodenum. Because epinephrine produces typical pain with great regularity in patients with angina pectoris, therapeutic use of the drug in such patients should be carried out with great caution.—Authors' Summary.

Studies on the hormone of the adrenal cortex (Recherches sur une hormone cortico-surrénale). de Mira, F. and J. Fontes, Compt. rend. Soc. de biol. **101:** 602. 1929.

An extract of entire adrenal gland made in salt solution and freed from adrenalin was injected into decapsulated rabbits. It was found to relieve muscular fatigue as tested by an ergograph.—J. C. D.

Similarity of action between histamine and adrenin on tired rabbit muscle (L'action de l'histamine sur les muscles fatigues du Lapin est semblance a celle de l'adrénaline).

Action of adrenin on tired muscles from decapsulated rabbits (Action de l'adrénaline sur les muscles fatigúes du Lapin décapsule). de Mira, F. and J. Fontes, Compt. rend. Soc. de biol. **102**: 209, 211. 1929.

Adrenin in small doses revives the fatigued extensor foot muscles in normal and decapsulated rabbits. Histamine in doses twice as great as those of adrenin produces the same results, which are due to an increased blood supply following capillary dilation. These results suggest that the power of cortical extracts to revive tired muscle, which is thought to indicate a cortical hormone, is actually the result of small traces of adrenin or some histamine-like product formed during the preparation of the extract.—J. C. D.

Action of the toxins of botulinus and of anaphylactic shock on the chemical composition of the adrenal (Action de la toxine botulique et du choc anaphylactique sur la composition chemique des surrénales). Mouriquand, G., A. Leulier and P. Sedallian, Compt. rend. Soc. de biol. **100**: 682. 1929.

The botulinus toxin reduces the amount of adrenin but not of lipoids when injected into guinea pigs; that of shock has no effect.—J. C. D.

Hyposuprarenalism. Peterman, M. G., Am. J. Dis. Child. **37**: 1238. 1929.

A case of possible hyposuprarenalism in a boy of 13 years of age is reported. The outstanding features were the history of tuberculosis and possible Addison's disease in the father's family and in the patient, the history of weakness, lassitude, easy fatigability, vaso motor instability, gastro-intestinal irritability, lowered resistance to infection, repeated attacks of acidosis, bronze skin, low blood pressure, sweating of the hands, hypoglycemia, acid intoxication and ketosis. Post mortem examination revealed an almost comp'ete destruction of the suprarenal glands by fatty degeneration.—M. B. G.

Adrenin and acidosis (Adrénaline et acidose). Raffiin, R. and P. Saradjichvili, Compt. rend. Soc. de biol. **102**: 560. 1929.

A study of the results of intravenous and subcutaneous injections of adrenin lead the authors to conclude that it produces retention of chlorine to a point approaching acidosis and an elimination of other acid ions in the urine.
—J. C. D.

Physiological studies of malignant cells (A preliminary communication). Sokoloff, B., Am. J. Physiol. **90**: 521. 1929.

A combination of iron and an extract of whole suprarenal gland was found to possesse the property of regulating the nucleo-cytoplasmic ratio of certain protozoa. Prolonged action of this material causes liquefaction of the protoplasm. The iron and suprarenal extract with the addition of tri-naphthypararosanilin sulphate was found to have a selective destructive action on the malignant cells of four types of tumors in mice and rats.—M. O. L.

Blood supply to suprarenals (Über die Blutversorgung der Nebennieren). Solotuchin, A., Ztschr. f. Anat. u. Entwcklngsg. **90**: 288. 1929.

It is suggested that some of the interrelations of the suprarenals and sex organs may be due to a common blood supply.—A. T. R.

The action of ephedrine on the blood sugar (with a note on its action on the denervated pupil of a cat). Teyko, E. and G. Mekes, J. Physiol. **68**: 247. 1929.

This substance increases blood sugar in rabbits. The antagonism for insulin is very weak in the rabbit but more pronounced in the dog; there is a synergy between ephedrine and epinephrine in the latter animal. Ephedrine did not affect the denervated pupil of a cat.—C. I. R.

The adrenal and pancreatic diabetes (Surrénale et diabète pancréatique). Turcatti, E., Compt. rend. Soc. de biol. **102:** 466. 1929.

In dogs, removal of the pancreas and adrenals together or at different times prevents the appearance of hyperglycemia during the short period the animals survive. Denervation of the adrenals does not prevent the appearance of diabetes.—J. C. D.

Adrenin as a factor in the dissociation of gasses in the blood (Rôle de l'adrénaline comme facteur de dissociation des gaz du sang). Vacek, T., Compt. rend. Soc. de biol. **102:** 267. 1929.

If potassium ferricyanide and adrenin are added to blood, there is more gas released than if ferricyanide alone is added. This is due to the adrenin regardless of its reaction. It would seem from these and other experiments that adrenin reacts with ferricyanide to form some gas, probably carbon dioxide.—J. C. D.

The alkaline reserve after adrenalin injections (La reserve alcaline apres injection d'adrenaline). Vallagnose, L., E. Herzfeld and J. Gautrelet, Am. J. Physiol. **90:** 543. 1929.

The alkaline reserve was measured in dogs by Van Slyke's volumetric method after the injection of 1/10 mgm. of adrenaline chloralose. There was almost immediately a marked increase (10-40 per cent) of short duration. Five minutes later the alkaline reserve reached its normal degree; it then lowered progressively. A drop of 40 per cent after two hours was recorded.
—J. Gagnon.

The reduction of the toxicity of adrenin by the hypotensive substance of the pancreas (Sur l'atténuation de la toxicité de l'adrénaline par la substance hypotensive du pancréas). Vaquez, P. Gley and N. Kisthinios, Compt. rend. Soc. de biol. **100:** 1088. 1929.

The authors have separated a blood pressure reducing extract which, while frequently present with insulin in commercial preparations, is an entirely distinct substance. When rabbits are treated with it, they are undamaged by otherwise lethal doses of adrenin.—J. C. D.

Choline and the adrenal capsule (Choline et capsules surrenales). Viale, G. and T. Combes, Compt. rend. Soc. de biol. **102:** 461. 1929.

Two dogs were decapsulated. Injections of adrenin failed to produce an increase of choline in the blood, as is the case in animals with intact adrenals. This is evidence that the adrenal cortex is the source of such choline. The vagus nerve on one side was cut sub-diaphragmatically in seven dogs, and, after twenty-one to sixty days, the choline content of the adrenal on the cut side estimated. Section of the vagus did not influence the choline content.
—J. C. D.

Utilizing the splenic contractions produced by adrenin in operations on the spleen (De L'utilisation de la spléno-contraction adrénalinique pour les opérations spléniques). Weil, P. E. and R. Gregoire, Compt. rend. Soc. de biol. **100:** 637. 1929.

In one case out of three, an injection of adrenin reduced the size of an enlarged spleen so that there was very little hemorrhage at operation.—J. C. D.

On the reversal of the effect of adrenaline upon the rabbit's intestine and the toad's limb vessels. Yen, T. J., Tohoku J. Exper. Med. **14:** 415. 1930.

In an elaborate 36-page table Yen reviews the literature on the reversal of the reaction to adrenaline in various organs with change of dosage or other conditions. He adds the results of a personal study of the phenomenon using rabbit intestine and the perfused leg of the toad. Reversal of reaction was infrequently seen in intestinal preparations supplied with air, but when adre-

naline aerated for 20-30 minutes was applied to the preparations reversal was invariably seen. It is ascribed to decomposition products of oxidized adrenalin. Very few instances of reversal of effect with change of dosage were seen in the toad-leg preparations.—R. G. H.

Influence of the thyroid, suprarenals and nervous system on production and treatment of peptic ulcer. Crile, G. W., Society Proceedings of the Southern Surgical Association, Dec. 10-12, 1929. Abst., J. A. M. A. **94**: 290.

Clinical and experimental evidence indicates that hyperacidity and hypermotility are controlled by the nervous system and the thyroid and suprarenal glands, which exhibit a reciprocal relation. The thyroid gland controls the permeability of every cell of the organism. The suprarenal glands are an integral part of the nervous system, especially of the sympathetic system, which in turn is the greatest activator of the thyroid gland. It is logical to expect, then, that gastric ulcer could be controlled by excision of sufficient thyroid or suprarenal tissue to reduce the drive of the sympathetic nervous system. A reciprocal, independent group of organs forming a working system apparently is best modified by removing a part of each. Accordingly, partial thyroidectomy and suprarenalectomy were performed in five cases of intractable or recurrent ulcer of the stomach, followed in every case by a decrease in gastric and intestinal motility and disappearance of the symptoms of ulcer.

The endocrine glands from procreation to death (Les glandes endocrines de la procreation a la mort). Levi L., Rev. franç. d'endocrinol. **7**: 294. 1929.

A review is given of some of the literature concerning the relation of the endocrines to human development from conception to death. The various endocrinopathies of the different ages, e. g., foetal life, pre-puberty, middle age and old age are discussed, and endocrine therapies which have proved helpful are described.—B. C.

Recklinghausen's disease and pluriglandular disturbances. Mosbacher, F. W., Arch. f. Psychiat. **88**: 163. 1929. Abst., J. A. M. A. **93**: 1422.

Mosbacher discusses the various aspects from which the etiology of the disease has been reviewed. Older authors have studied the microscopic changes; recently the problem has been brought up in connection with disturbances of internal secretion. The case reported may be considered as representing a typical example of this interrelation, and Mosbacher infers that the conception of neurofibromatosis must be extended to include the simultaneous occurrence of endocrine disturbances and to consider all cases in which this is not evident as exceptions. The history of the patient revealed hereditary insanity. One of his brothers was nervous and one was slightly acromegalic; two others were without taint. Up to his eighteenth year the patient was perfectly normal; marked growth of his hands and feet then occurred and he was subject to attacks of melancholy. Lack of concentration, impatience, fidgeting, excitement and other symptoms of mental disturbance, together with headaches and pain in the region of the kidneys, were present. Histologic examination of a small tumor obtained from the left arm presented the picture of a neurofibroma. The basal metabolism was considerably disturbed, which together with the symptoms of acromegaly was characteristic for hyperfunction of the pituitary body and thyroid. The deficient development of secondary sexual characteristics indicated involvement of the genital glands, and diffuse pigmentation of the skin was symptomatic for participation of the suprarenals. To which of these symptoms the slight mental disorder should be ascribed, was not clear; however, the hereditary factors may be partly responsible.

Heteroplastic pluriglandular grafts on man as treatment of endocripopathies (Impianti pluriglandolari eteroplestici nell'uomo per la cura dell Endocrinopatie). Pende, N., Rass. Clin. Scient. Ist. Biochim. It. **6**: 3, 1928.

The author takes a firm stand against the theory of rejuvenation, while he believes it possible to delay by grafts the senescence, not of one but of several endocrine glands. The treatment is indicated for delayed somatic, psychic and sexual development in adolescent subjects with endocrine alterations and also for amenorrhea due to hypoovarism or hypoovarism and hypopituitarism and for adiposity of hypophyseal, ovarian or thyroid origin. The

conclusions of the author on his 14 cases are that the effect is not promptly seen. At times it takes 3 to 4 months before it shows. The technic must be correct and should not give any reaction of fever. The only phenomenon happening almost constantly and without serious consequences is a crisis of polyuria and arterial hypotension on the day following the operation. The operative wound heals remarkably quickly. As to the good effects of this treatment there cannot be any doubt, when following it, a woman who had her menopause 22 years before actually had reappearance of menstruation for over two years. Rather than to attribute the good effect to absorption of autolytic material derived from the grafted glands Pende believes in a reduced vitality of the glands, which allows them a certain degree of hormonic functionality. The effect of such grafts is only temporary (one year or more, according to Pende's observations), but in spite of it their usefulness is beyond doubt. As a final conclusion the problem of the pluriglandular graft is based on the correct endocrine diagnosis of the patient and on the consequent rational therapy. Monkey glands (hypophysis, thyroid or gonads) are used, grafted around the external vaginal coat of the testes and in women in the deep retro-mammary tissue.—G. V.

Constitution and human races (Konstitution und Rasse beim Menschen). Saller, K., Ergebn. d. Anat. u. Entwcklngsg. **28**: 250. 1929.

In connection with a discussion of the factors underlying constitutional types, there is a brief review of some of the speculations that have been advanced regarding the rôle of the various endocrine organs in determining these characteristics.—A. T. R.

The internal factors of development. Hormones and the nervous system (Les facteurs internes de la croissance. Hormones et systeme nerveaux). Aron, M., Rev. franç. d'endocrinol. **7**: 269. 1929.

The current views of the hormone control of development are reviewed. Evidence is presented, based upon grafting experiments, that two regions of the central nervous system are especially involved in development. Early development through germ layer formation may be controlled by the innate power of the fertilized ovum. After the formation of the nervous system the control passes to it, and when the endocrines originate, at least in certain Amphibians, control is partly invested in them.—B. C.

Cryptorchism in horse, pig, dog and cat, histological study (Untersuchungen über Kryptorchismus beim Pferd, Schwein, Hund und bei der Katze, under besonderer Berücksichtigung der mikroskopischen Anatomie). Bötschi, A., Ztschr. f. Anat. u. Entwcklngsg. **89**: 727. 1929.

Largely of morphological interest. The author does not agree entirely with the idea that adult retained testes are essentially of a juvenile or foetal type.—A. T. R.

A new test for normal and experimental changes occurring during the oestrous cycle in guinea pigs (Un test nouveau des modifications spontanées et provoquées de l'oestrus chez la Souris). Bourg, R., Compt. rend. Soc de biol. **102**: 592. 1929.

Histologically the lipoid granules in the cells of the uterine epithelium of guinea pigs and rats undergo cyclic changes during oestrous. They disappear during preoestrous and reappear in metoestrous. These same alterations occur when the cycle has been brought on in a spayed animal by the use of folliculine.—J. C. D.

Compensatory hypertrophy of the untreated ovary after unilateral X-ray sterilization. Brambell, F. W. R. and A. S. Parkes, Proc. Roy. Soc. B. **105**: 36. 1929.

In each of 107 mice, 4 weeks old, the right ovary was sterilized by irradiation. The left ovaries underwent complete compensatory hypertrophy as judged by weight of the ovary and size of the litter. The number of follicles maturing at each oestrus and the number of resulting corpora lutea were approximately equivalent to those of two normal ovaries.—E. L.

Decidual reactions of the mucous membrane of the uterus and their connection with the internal secretion of the ovary (Réactions déciduales de la muqueuse utérine et leurs rapports avec la sécrétion interne de l'ovaire. Brouha, L., Liége méd. **21**: 1211. 1928. Abst., Rev. franç. d'endocrinol. **7**: 324.

In order that the gravid transformation of the uterine mucous membrane may take place there must be the action of two hormones taking place, folliculine and the hormone secreted by the corpus luteum acting in a definitely established time relation.—Translated by J. Gagnon.

Effects of urine from pregnant women on the male genital tract (Action de l'urine de femme gravide sur de tractus génital male). Brouha, L. and H. Simonnet, Compt. rend. Soc. de biol. **101**: 368. 1929.

Male mice received daily for ten days injections of urine from a two months pregnant woman. In young mice, genital growth was hastened, particularly that of the accessory sex glands. In adults, these glands hypertrophied. This is a more delicate test for pregnancy than the changes produced in the female mouse. The changes may be due to anterior hypophysis substance in the urine. After three months pregnancy, folliculine becomes prominent in the urine and overshadows the hypophyseal secretion, so that such urine then has an inhibitory influence on the genital tract.—J. C. D.

Effect of the age of the recipient and of the grafted ovary on the oestrous cycle in the white rat (Influence de l'age de l'animal récepteur et de l'ovaire greffé sur le cycle oestral du Rat blanc). del Castillo, E. B., Compt. rend. Soc. de biol. **102**: 457. 1929.

Adult ovaries grafted into adult hosts thrive best and survive up to one and a half years. Immature ovaries grafted into adult hosts grow for a while but are eventually absorbed, while adult ovaries in hosts before puberty do not grow. The hosts were spayed. The transplants were made into the kidney. The effectiveness of the grafts was judged by the vaginal smears. The presence of grafted ovarian tissue was confirmed by autopsy.—J. C. D.

The basal metabolic rate in relation to the menstrual cycle. Conklin, C. J. and J. F. McClendon, Arch. Int. Med. **45**: 125. 1930.

From a study of 10 subjects it was concluded that the basal metabolic rate tends to reach its lowest level following menstruation and its highest level preceding menstruation. A deficient diet decreases not only the basal metabolic rate but also the duration of menstruation and the length of the menstrual cycle.—R. G. H.

Neutralization of the follicular hormone in a pregnant female which was spayed (Neutralisation de l'hormone folliculaire chez la femelle gesante castrée). Courrier, R., R. Kehl and R. Raynaud, Compt. rend. Soc. de biol. **100**: 1103. 1929.

Guinea pigs will carry fetuses to normal delivery, if spayed late in pregnancy. Folliculine injected into a spayed, but not pregnant animal, produced vaginal changes in three days. When injected into a pregnant female it had no effect. It produced no vaginal changes in a spayed pregnant female. This result indicates that there may be some mechanism besides the corpus luteum to neutralize folliculine in the pregnant animal.—J. C. D.

Observations on the standardization of the water-soluble oestrus-producing hormone. Dickens, A. T. and E. C. Dodds, J. Physiol. **68**: 348. 1930.

Detailed outlines of precautions necessary are given, including strict asepsis in ovariectomy, diet and standard technic. Injections were made twice daily during these days of 0.2 cc. of the extract. Vaginal smears were made on the first and second days and twice on the third and fourth days, the last three smears being mixed with a drop of water. Evaluation of smears is discussed in detail. Other methods of administration are also discussed.—C. I. R.

The simultaneous production of two hormones by the corpus luteum. Frank, R. T., R. G. Gustavson, Helen McQueen and M. A. Goldberger, Am. J. Physiol. **90**: 727. 1929.

The same batch of pink corpora lutea of the sow was extracted with alcohol and then extracted by the technic described by Hisaw (dialyzation through collodion membrane). The ether fraction was injected into castrated rats and gave a positive reaction for the presence of the female sex hormone. The aqueous fraction gave a positive test for the presence of the corpus luteum hormone (weakening the symphysis pubis of the virginal guinea pig). It is thus demonstrated that the corpus luteum contains two different hormones, the one corresponding to that of the follicle and the placenta, the other a cycle inhibiting and nidatory hormone.—R. T. Frank.

The significance of the occurrence of oestrin in male urine. Free, A. R., G. F. Marrian and A. S. Parkes, J. Physiol. **67**: 377. 1929.

A substance was extracted from male urine that is identical in physiological action with oestrin as indicated by vaginal cornification and uterine hypertrophy. The kidney does not actively secrete or concentrate this substance. Oestrin added to the heart-lung-kidney preparation is not excreted or absorbed and does not disappear when incubated with shed blood. Disappearance when injected is due to oxidation.—C. I. R.

Studies in ovulation. I. The relation of the anterior pituitary body to ovulation in the rabbit. Free, A. R. and A. S. Parkes, J. Physiol. **67**: 383. 1929.

Hypophysectomy within an hour after copulation inhibits ovulation.
—C. I. R.

Physiology of corpus luteum. IV. Production of artificial deciduomata with extracts of the corpus luteum. Goldstein, L. A. and A. J. Tatelbaum, Am. J. Physiol. **91**: 14. 1929.

Bilateral ovariectomy and traumatization of the uterine mucosa were performed on virgin guinea pigs on fifth day after oestrus and followed by five daily subcutaneous injections of either corpus luteum extract (as prepared by Corner and Allen), or estrogen, or mazola oil. Autopsies were performed on the sixth day after operation. Deciduomata were formed at point of trauma in those animals treated with corpus luteum extract. The animals treated with estrogen and mazola oil showed no growths. Deciduomata were also produced in normal animals (with ovaries intact and no injections) by similar traumatization. The experiments confirm the observation that corpus luteum extract contains a special hormone which has for one of its functions the sensitization of the uterine mucosa of the guinea pig so that deciduomata are formed upon indifferent stimulation of the endometrium during the proper period of the sexual cycle.—L. A. Goldstein.

Ovarian follicular hormone. Janney, J. C., Arch. Surg. **18**: 1241. 1929.

The work reported is based on 203 injections of castrated female white mice in an effort to confirm the dependability of the blood test for oestrus-producing hormone as previously reported by Frank and Goldberger. The technic of the experiments was, with one or two exceptions, kept as nearly identical with Frank's technic as was possible. The reason for the changes made has been fully discussed. Frank's method of reading the smears has been followed. The curve obtained from the pregnant patients, from whom blood was obtained for control, approximated the results already reported by Frank. The curve obtained from the bloods secured at various periods of the menstrual cycle did not agree in any of the essential particulars with Franks' results and the blood test is considered too unreliable for clinical use. Although this series is larger than the number reported by Frank neither one, nor the combination, is sufficiently large to form a dependable criterion of the reliability of the test.—Author's Abst.

Effect of castration on muscle (Influence de la castration sur la musculature). Jasienski, J., Compt. rend. Soc. de biol. **101**: 533. 1929.

The author studied cattle, guinea pigs, chickens, rabbits and frogs. The striking changes were best shown by steers and frogs and consisted of a marked reduction in the diameter of the individual muscle cells in the castrates.
—J. C. D.

Production of precocious puberty by parabiosis (Puberté précoce par parabiose). Kallas, H., Compt. rend. Soc. de biol. **100**: 979. 1929.

Sixteen female albino rats, 15 to 20 grams in weight, were parabiotically united to spayed females of the same age. The vagina opened 7 to 9 days later and the oestrous cycle was established. This early maturity is considered as due to the double quantity of pituitary hormone acting on a single set of ovaries.—J. C. D.

Precocious development of the genitalia in male rats by parabiosis (Développement précoce de l'appareil génital chez le Rat male infantile en parabiose). Kallas, H., Compt. rend. Soc. de biol. **102**: 552. 1929.

Pairs of young rats, one of which was a normal male and the other a gonadectomized animal of the same age, were united by parabiosis. Abnormally rapid sex development of the normal male took place, which was identical with that produced by transplants of the pituitary. This result followed whether the gonadectomized animal was male or female.—J. C. D.

Rut and the corpus luteum (Rut et corps jaune). Lipschütz, A. and L. Adamberg, Compt. rend. Soc. de biol. (Paris), **102**: 282. 1929.

Guinea pigs were subjected to spaying and then to implantation of ovarian tissue into the kidney. They showed active oestrous followed by prolonged four months dioestrous. The grafts showed corpora lutea and large follicles. These latter were of such size that they could be regarded as active endocrine organs. Evidently then the secretion of the corpora lutea blocked the action of the follicular hormone, possibly by a desensitizing action on the uterus, vagina, etc.—J. C. D.

Compensatory reactions of the testicle of the guinea pig after unilateral castration (Réactions compensatrices du testicule du cobaye après castration unilatérale). Lipschütz, A. and E. Viñals, Compt. rend. Soc. de biol. **100**: 984. 1929.

Testicular weight has been compared in normal and unilaterally castrated animals of the same litter 9 to 13 months after birth, the operation having been performed several days after birth. In the majority of cases testicular weight was greater in the experimental animals. There were 2 cases in which the testicle attained a weight which was 72 and 94 per cent higher than that of one normal testicle in the control animal. But if the weight as attained by the testicle in the experimental animals is compared with the maximal weight in normal animals, then there were only 4 cases in which testicular weight in the experimental animal was greater, whereas in 9 cases testicular weight was not beyond normal maximal weight. The difference between the experimental maximum and the normal maximum was only about 20 per cent. These data are in favor of the theory that compensatory hypertrophy of the testicle after unilateral castration is to be explained by acceleration of growth in such a manner that the maximal testicular weight in unilaterally castrated adult animals is sooner attained than is the case in normal ones. The extratesticular factor responsible is probably the hypophysis.—A. Lipschütz.

Compensatory reactions of the ovary of the guinea pig after unilateral castration (Réactions compensatrices de l'ovaire du cobaye après castracion unilatérale). Lipschütz, A., Compt. rend. Soc. de biol. **100**: 986. 1929.

Former experiments suggested that hypertrophy of ovarian fragments is an integrative phenomenon based on the law of follicular constancy. This makes it probable that ovarian hypertrophy can be explained on the same lines as testicular hypertrophy in mammals. One hundred fifty-nine ovaries

of the guinea pig at different ages have been weighed. The maximal ovarian weight is by no means attained at puberty. The relation between the maximal and the minimal ovarian weight varies according to age or body weight, being 7.7 at a body weight of 100 to 200 grams and 2.7 at a body weight of 600 to 700 grams. Evidently the possibilities of attaining the maximal weight are quantitatively characteristic of each age and these possibilities are greater the older the animal. In unilaterally castrated animals the difference between the experimental and the normal minimal ovarian weight was 81 per cent; on the contrary, the difference between experimental and the normal maximal weight was only 31 per cent. Evidently the possibilities of attaining the maximal ovarian weight characteristic of a certain age are greater when only one ovary is present. All these data can be dynamically understood if the law of follicular constancy is taken into consideration. The maximal ovarian weight after unilateral castration can indeed be greater than the normal maximal ovarian weight; but the difference between the experimental and the normal maximum is not very pronounced and from a dynamic point of view the difference can be explained as caused by the fact that the ovary in the unilaterally castrated animal reaches the potential normal maximum sooner. The same general principles underlie the compensatory reactions in the testicle and in the ovary.—Author's Abst.

Folliculine and diuresis (Folliculine et diurèse). Lipschütz, A. and E. A. Wilckens, Compt. rend. Soc. de biol. **102**: 553. 1929.

Spayed guinea pigs were injected with folliculine alone or with folliculine and quantities of fluid, which would promote diuresis. The oestrous cycle was re-established and persisted for the same length of time, regardless of whether fluid was injected with the folliculine or not. Since an increased output of urine does not reduce the effect of the folliculine on the oestrous cycle, little of the folliculine is eliminated through the kidneys under normal conditions. The elimination of large quantities in the urine during pregnancy must be regarded as a response to special conditions.—J. C. D.

The assay of oestrin. Marrian, G. F. and A. S. Parkes, J. Physiol. **67**: 389. 1929.

A method for a standardization is described with a discussion of the variable factors.—C. I. R.

The treatment of endocrine disturbances in menstruation. Martin, F., Deutsche med. Wchnschr. **54**: 989. 1928.

The disturbances in menstruation considered are irregular and profuse flow in individuals in whom there is no pathological change in the uterus or ovaries. The extent of the dysfunction of any particular component of the endocrine system can not be measured. Therefore, it is a matter of chance whether one can treat that portion of the organ complex which is at fault. Rather than attempt to regulate the individual components of the endocrine system, the author advocates stimulation of metabolism by improving the living conditions, which refers to place of abode, climate, habits, state of nutrition as well as psychic factors. Four cases are reported in which no specific medication was used, but unsatisfactory hygienic conditions were corrected with the result that the symptoms are relieved.—M. R. White.

Exchange of hormones in animals in parabiosis. Passage of the ovarian hormone from the normal to the spayed animal (Exchanges hormonaux chez les animaux en parabiose. Passage de l'hormone ovarienne des sujets normaux aux sujets chatrés).

Oestrous cycle in normal and spayed rats in parabiosis (Cycles oestraux chez les rats normaux et chatrés vivant en parabiose). Martins, T., Compt. rend. Soc. de biol. **102**: 605, 614. 1929.

When a pair of female rats, one spayed and one normal, are united by parabiosis, the normal animal shows a prolonged break in the oestrous cycle. This is followed by the appearance of cyclic changes in the vaginas of both

animals showing that the ovarian hormone passes from the normal to the spayed animal and influences its genital tract. The ovaries of the normal animal are enlarged and present a picture similar to that following administration of anterior lobe substance. The uterus of the spayed rat is undersized but not atrophic to the extent found in untreated spayed animals. The guinea pig shows similar evidence of the passage of ovarian hormone.—J. C. D.

The seminal vesicle of the white mouse as a test for the testicular hormone (Utilisation des vésicules séminales de la Souris blanche comme test des hormones testiculaires). Martins, T. and A. Rocha e Silva.

Action of testicular extracts on the vesicles of castrated mice (Action des extraits testiculaires sur les vésicules séminales des Souris chatrées). Martins, T. and A. Rocha e Silva, Compt. rend Soc. de biol. **102:** 480, 485. 1929.

Following castration, within five days, there are marked cytological changes in the vesicle. In less than two weeks, there is marked shrinkage of the entire vesicle. Using the product of length times width as an index, this index falls to half its former value. These changes can be prevented by injections of extract from bull and goat testis. The article is illustrated. Directions for making the extract by treatment with alcohol, benzol, and subsequent saponification are given. This work agrees with that of Moore and Gallagher on the white rat, published about the same time.—J. C. D.

Induction of menstruation in women by use of ovarian hormone. McClendon, J. F., G. Burr and F. F. Wildebrush, Proc. Soc. Exper. Biol. & Med. **26:** 430. 1929.

In a case of amenorrhea of 5 months duration in a woman 19 years old the injections of 1000 mouse units of ovarian hormone daily for 9 days was followed by a menstruation three weeks later. In a second case of 5 years duration in a woman 22 years old a menstruation occurred after two series of injections totalling 15,000 mouse units.—M. O. L.

A case of eunuchoidism (Uber einen Fall von Eunuchoidismus). Munro, Ztschr. f. Konstit. **14:** 401. 1928.

The report concerns a man of 59 described largely from postmortem examination. There was absence of body hair, marked hypoplasia of the testis and moderate hypoplasia of the external genitalia. There was tallness, moderate prognathism, and marked atrophy of the prostate. Numerous anthropological measurements are given which show that this is a typical case of eunuchoid tallness with the disproportions of the condition, such as greater length of the lower part of the body when compared with the upper part, increased span of the arms, delicate bones, long thin extremities, relatively wide pelvis and very small shoulders. On histological examination the testis was seen to consist of a great overgrowth of interstitial cells, with atrophic seminiferous tubules. The thyroid and adrenal were somewhat hypoplastic.
—W. J. A.

Influence of the sex hormones on the basal metabolism. Experiments with females (Influence des hormones sexuelles sur le métabolisme basal. Essais expérimentaux chez les femelles). Ptassek, L., Compt. rend. Soc. de biol. **100:** 1250. 1929.

In bitches, as in male dogs, castration results in a decline in the basal metabolism, followed by a temporary return toward normal, and then a fall in metabolic rate. This is then maintained permanently at 50-60% of the original rate.—J. C. H.

Gynecomastia (Zur Kenntnis der Gynäkomastie). Schmidt, O., Ztschr. f. Konstit. **14:** 588. 1929.

From the literature, the author gathered 179 cases of gynecomastia. A great many of them had genital disorders; 47 of them were examined anatomically and proven to be cases of actual hypertrophy of the mammary gland.

Of the thirteen cases in which the testes had been examined histologically, eight showed testicular atrophy and four contained tumors. This suggests some relation between gynecomastia and abnormal testes, although there is also much to be said for the chromosomal origin. Many cases had other endocrine disorders that might influence the testes and thus indirectly be related to the hypertrophy of the male mammary gland. Twenty-four additional cases were found in the Russian literature too late to be included in the analysis.
—A. T. R.

Significance of the blood supply, internal pressure and interstitial cells in the biology of the testis (Über die Bedeutung der Vascularisation, des Binnendruckes und der Zwischenzellenfür die Biologie des Hodens). Schweizer, R., Ztschr. f. Anat. u. Entwcklngsg. **89**: 775. 1929.

A discussion of the rôle of the blood supply, structure and position of the testis in spermatogenesis. The interstitial cells are considered factors in regulating the blood supply by exerting direct pressure on the small vessels and by modifying the general internal pressure in the testis as a result of their atrophy and hypertrophy.—A. T. R.

Clinical observations on the use of an ovarian hormone; Amniotin. Sevringhaus, E. L. and J. S. Evans, Am. J. Med. Sc. **178**: 638. 1929.

The effect of amniotin, an ovarian hormone secured from the amniotic liquor of cattle, has been studied on 25 women with menopausal and menstrual disturbances. Its use has been of marked value in the relief of the vasomotor phenomena of the menopause, and in promoting feminine development of one woman of infantile type.—Authors' Summary.

Comparative morphology of the interstitial tissue of mammalian testis (Zur vergleichenden Morphologie des Zwischengewebes im Säugerhoden). Silbermann, U., Ztschr. f. Anat. u. Entwcklngsg. **90**: 597. 1929.

A description is given of the histology of the interstitial tissue of about 14 species.—A. T. R.

Sex glands and adaptive ability. Tsai, L. S., Science, **71**: 106. 1930.

The experiments deal with the effect of castration upon problem box and maze performances by white rats. At the age of about five months, twelve rats had both of their testicles removed (total castration), eight had only one testicle removed (semi-castration), and seven were put through a control operation. After one week of preliminary training, they were required to solve a single-platform box problem once a day for four weeks. Then they were given a week of preliminary training in the maze which they were required to learn once a day during the next two weeks. The maze experiment was repeated on eight totally castrated and eight control animals for four weeks. The results indicate that the totally castrated rats are inferior to the semi-castrated and the control animals in their adaptive ability as measured by the speed in solving the problem box as well as by both speed and accuracy in maze performance.—Author's Abst.

On the pregnancy-response of the uterus of the cat. Van Dyke, H. B. and R. G. Gustavson, J. Pharmacol. & Exper. Therap. **37**: 379. 1929.

If the hypogastric nerves of the cat are stimulated, it is well known that the non-pregnant uterus relaxes, while the pregnant uterus contracts. The attempt has been made to cause this pregnancy-response in ovariectomized and non-ovariectomized virgin or non-pregnant cats by the subcutaneous administration of various extracts. The following results were obtained: Ovariectomy did not alter the response of the non-pregnant cat's uterus. Ovariectomy in the pregnant cat, accompanied in our experiments by fetal resorption was without effect unless fetal resorption was complete. In the latter case the uterus behaved like a non-pregnant uterus. A foreign body introduced into the non-pregnant uterus had no effect on the response. Placental and follicular-liquid extracts provoked marked uterine hypertrophy without any

pregnancy-reversal of the uterus. Extracts of early vascularized and late vascularized corpora lutea, ovarian residue, uterus and fetus caused little or no uterine hypertrophy and no alteration of response. Lipoidal extracts of mature corpora lutea caused pronounced uterine hypertrophy in experiments with three kittens. A contraction of the uterus simulating pregnancy repeatedly occurred in two of these experiments when the hypogastric nerves were stimulated. Aqueous extracts of mature corpora lutea administered with placental hormone also caused this reversal simulating pregnancy in two of three animals. This effect seemed specific for corpus-luteum extract and probably was due to a substance other than that provoking estrus.

—Authors' Summary.

The dosage and action of pituitary extract and of the ergot alkaloids on the uterus in labor, with a note on the action of adrenaline. Bourne, A. and J. H. Burn, J. Obstet. Gynec. Brit. Emp. **34**: 249. 1927. Abst., Physiol. Absts. **14**: 402.

Observations were made on patients in labor. A small rubber bag was inserted with aseptic precautions into the uterus between the membranes and the wall, past the head of the foetus. A record of the pressure changes inside the bag was obtained by way of a manometer on a moving drum. It was found that in a series of 12 primiparous patients a dose of 2 units of pituitary extract, injected during the first stage of labor, never produced untoward effects. Provided the os was at least half dilated, the increase in uterine contractions was usually great enough to shorten the course of labor materially. Tyramine, even in a dose of 10 mgm. given intravenously, produced only a trace of effect on the uterus. Histamine given subcutaneously in doses of 1 mgm. (base) temporarily quickened the rate of contraction, but the effect of even 2 mgm. did not last more than 45 minutes, and the response to this dose was great enough in force to lead to subsequent exhaustion. Ergotamine in doses up to 1-10 mgm. produced a prolonged increase in the tone of the uterus, so that there was no full relaxation between each contraction. The effect of ergot preparations must therefore depend on the amount of specific alkaloid present, and not on histamine and tyramine. Evidence is given showing that ordinary clinical methods do not suffice to distinguish between active and inactive extracts. It is shown that ether inhibits the contractions of labor, though not the contraction produced by ergotamine. It is also shown that adrenaline (0-3 cc.) intravenously inhibits the contraction of the uterus in labor.

Oxytocin and vasopressin. A further examination of the separated principles of pituitary (Posterior Lobe) extract. Burn, J. H., Quart. J. Pharmacol. **1**: 509. 1928.

The two principles, Oxytocin and Vasopressin, separated from posterior lobe, were examined as to distribution of the antidiuretic and insulin-inhibiting properties. The antidiuretic effect was studied on a human by a method described by the author in the same issue (p. 496), consisting of finding the time required to reach a maximum rate of urine excretion after drinking a liter of water simultaneously with subcutaneous injection of the extract to be tested. Pituitrin was used as a standard of comparison. A chart is given showing that not more than a trace of antidiuretc activity is present in Oxytocin, while Vasopressin has this activity to the same extent per unit of pressor activity as has Pituitrin. The inhibiting effect upon the hypoglycemic action of insulin was determined by injecting insulin plus the extract to be tested into a starved rabbit. Hourly blood sugar values were compared with those obtained one week later in the same rabbit when given insulin alone. A table and chart are given to show that Oxytocin has no power to prevent the hypoglycemic action of insulin, while Vasopressin has a considerable effect. Only one rabbit was used for each test.—I. W. Grote.

Effect of insulin on the precocious puberty produced by hypophyseal transplants (Action de l'insuline sur l'apparition de la puberté précoce provoquée par implantation d'hypophyse). del Castillo, E. B. and C. Calatoni, Compt. rend. Soc. de biol. **102**: 455. 1929.

Daily doses of one insulin unit did not retard the rapid appearance of puberty following pituitary transplants in four white rats.—J. C. D.

The action of posterior pituitary pressor extract on the rabbit's vascular system. Clark, G. H., J. Physiol. **68**: 166. 1929.

Rabbits fed on dried thyroid for 14 days or more invariably died shortly after intravenous injection of pituitary extract in amounts that gave no obvious symptoms in normal rabbits. Oxytocin was not effective, the results being due to Pitressin. Death was due to cardiac depression. This was not due to vagal activity; the author suggests that the extract affects the coronary vessels. The reason for thyroid sensitization was not determined.—C. I. R.

A crystalline substance of the hypophysis which promotes follicular growth. Claus, P. E., Proc. Soc. Exper. Biol. & Med. **27**: 29. 1929.

A crystalline product insoluble in absolute alcohol was prepared from the anterior lobe of the hypophysis, which induced precocious sexual maturity when injected in aqueous solution into 18-day-old mice. Another fraction from the anterior lobe soluble in absolute alcohol did not induce precocious sexual maturity but did promote lutein tissue formation and disintegration of ova in the ovaries.—M. O. L.

On the way extracts of the anterior lobe of the hypophysis act (Sur le mode d'action des extraits hypophysaires antérieurs). Courrier, R. and R. Kehl, Compt. rend. Soc. de biol. **100**: 711. 1929.

Alkaline extracts of bovine glands in small doses produce in cats follicular development in the ovary with characteristic accompanying changes in the genital tract. Heavy doses result in a corpus luteum like degeneration of the ripe follicles.—J. C. D.

Possible water balance; effects of alkaline anterior pituitary extracts. Downs, W. G. and E. M. K. Geiling, Proc. Soc. Exper. Biol. & Med. **27**, 63. 1929.

Mice receiving alkaline extracts of the anterior lobe gain weight more rapidly than do the controls, but their tissues contain from 6% to 8% more water and about 3% less ash than the tissue of controls.—M. O. L.

Pituitary extract and the CO_2 combining power of the blood plasma. Draper, W. B. and R. M. Hill, Proc. Soc. Exper. Biol. & Med. **27**: 33. 1929.

In normal dogs the intravenous injection of commercial pituitary extract is followed immediately by a marked fall in the CO_2 combining power of the blood plasma. Both the oxytocic and pressor principles of the posterior lobe produced this acidosis.—M. O. L.

On the ocytocic properties of blood from a woman in labor (Sur les propriétés ocytociques du sang de la Femme en travail d'accouchement). Fontes, J., Compt. rend. Soc. de biol. **102**: 227. 1929.

The uterus of a guinea pig was divided and each horn exposed to identical conditions except that one was bathed in defibrinated blood from a woman in labor and the other in blood from a man. The blood from the woman produced active and sustained contractions, that of the man had little effect. Blood taken from a woman eight days after delivery lacked ocytocic properties.—J. C. D.

Studies in Water Diuresis. II. The excretion of urine after hypophysectomy and decerebration. Free, A. R., J. Physiol. **68**: 305. 1929.

Total hypophysectomy followed by decerebration did not increase urine output or chloride excretion. Alimentary diuresis occurs normally in the decerebrate, hypophysectomized animal and is inhibited by pituitrin. If the operation was followed by renal denervation, large amounts of hypotonic urine were produced. Pituitrin reduced this and increased the chloride percentage.—C. I. R.

Diabetes insipidus and lesions of the mid-brain. Report of a case due to a metastatic tumor of the hypothalamus. Futcher, T. B., Am. J. Med. Sc. **178**: 837. 1929.

A case of diabetes insipidus due to an alveolar carcinoma of the hypothalamus, secondary to a primary carcinoma of the lung, and without an involvement of the pituitary, is reported. The case would naturally tend to support the view held by many that diabetes insipidus is due to a disturbance of certain regulatory centers in the hypothalamus. The studies supporting the pituitary and hypothalamic conception of the origin of the disease are reviewed. Reference is made to the fact that it now seems amply demonstrated that there are definite nerve fibers connecting the tuber cinereum and the posterior lobe of the hypophysis. The belief is expressed that, although there may be certain centers in the hypothalamus regulating water exchange in the body, the evidence seems very strong that disturbance of the action of a diuretic-antidiuretic hormone produced in the posterior lobe of the pituitary is a very important factor in the etiology of the disease, possibly by sensitizing these centers or by influencing their functions.—Author's Summary.

The effect of the hormone of the hypophysis on water and salt economy in persons with normal kidneys and diseased kidneys (Uber die Wirkung des Hypophyseninkretes auf Wasser und Kochsalzhaushalt von Nierengesunden und Nierenkranken). Gutmann, H., Arch. f. Verdauungskr. **42**: 551. 1928.

Patients with normal kidney function and normal blood pressure were chosen for the experiment. They were given 1 liter of tea, but no food at seven o'clock in the morning. Urine was passed at half-hour intervals and the amount, specific gravity and sodium chloride content were recorded and plotted on a chart. In a later experiment the same procedure was followed except that fifteen minutes before the ingestion of the 1 liter of fluid an intramuscular injection of 2.0 cc. Pituglandol was given. In the control experiment the total urinary output and the specific gravity indicated increased excretion in the first hour. When Pituglandol was injected there was water retention reaching the maximum 1½ hours after the injection. The initial diuresis observed in animals given Pituglandol was not seen in these human subjects. While the water retention lasted the sodium chloride percentage was increased and the specific gravity was correspondingly increased. The duration of the water retention phase was from 2½ to 5 hours. Following the water retention phase there was a phase of compensatory diuresis during which a large volume of dilute urine was passed. After several hours the total urine and total salt excretion were the same whether the patient had been given Pituglandol or had not been injected. Five cases of kidney sclerosis with moderately high blood pressure were tested. In the first of these, after the 2 cc. injection of Pituglandol had been given, the total urine excreted in 12 hours was 800 cc., whereas in a previous test without Pituglandol the urinary output was 950 cc. After an injection of Pituglandol there was a phase of water retention similar to that observed in normal patients after the same treatment. The phase of compensatory diuresis was slower in coming on in these cases with kidney disease than in normal patients. It was evident that although the Pituglandol effect lasted longer, it was not as pronounced in these patients with kidney disease as in normal patients. Later experiments on patients with more badly diseased kidneys demonstrated the fact that the greater the kidney disturbance the less was the action of Pituglandol. The author does not consider it proved, however, that the pituitary hormone acts directly upon the kidney.

—E. P. Bugbee.

The anti-diuretic effect of the separated principles of the pituitary body. Hemingway, A. and J. M. Peterson, J. Physiol. **68**: 238. 1929.

The effects of pitocin and pitressin on water diuresis in man and on heart-lung-kidney preparations were investigated. By the latter method both caused decreased urine volume and increased concentration of chlorides. Pitressin is a vasoconstrictor to the renal vessels. After the ingestion of a liter of water in man, diuresis was inhibited.—C. I. R.

Simmond's disease (La maladie de Simmonds). Herman, C., Rev. franç d'endocrinol. **6**: 301. 1928.

A woman with a condition diagnosed as Simmond's disease presented an unusual physiognomy with a general appearance similar to that of a mummy.

The eye-brows were completely absent and the teeth had been lost, and there was thinning of the hair of the head and pubes. She showed a diminution in intelligence which was thought to be due to the nutritional changes. Treatment with thyroid extract had been without benefit. The author then treated the patient with an extract of the anterior lobe of the hypophysis by daily injecions, and noticed improvement in the psychic condition, although the disease continued. The patient's appetite was greatly improved and intense hunger was felt two to three hours after each injection. There was increased growth of the nails and of the hair in the axillary and pubic regions. The author believes that such a condition is caused by disease of the anterior hypophysis and that it is frequent in women at about the time of the menopause.—R. C. Moehlig.

The exchange of hypophyseal substance in parabiosis (Sur le passage de substances hypophysaires pendant la parabiose). Kallas, H., Compt. rend. Soc. de biol. **102:** 280. 1929.

Young female rats were united in pairs and one of each pair was spayed. Study of these showed that the precocious puberty induced in the unspayed animals of these pairs was marked by a transitory stage of active oestrous, followed by a prolonged dioestrous. The appearance of this latter condition could be accelerated by injections of hypophyseal extract into the spayed animal. This is further evidence of the passage of hypophyseal substance from one animal to another in parabiosis.—J. C. D.

Further researches on the anterior lobe pituitary hormone (Weitere Untersuchungen über das Hypophysenvorderlappenhormon: Prolan). Laquer, F., Am. J. Physiol. **90:** 424. 1929.

The anterior lobe of the pituitary can cause an early maturity of the sex organs, particularly the ovaries, in young female rats. Upon this fact Zondek and Aschheim base their test for the anterior lobe pituitary hormone. They have also found that this hormone is excreted in the urine during pregnancy. Researches concerning this have shown that young rats are in many respects better for the demonstration of the hormone than are young mice. Some of the chemical properties of the hormone are already known, particularly its great sensitivity to acids and alkalies, as well as its instability at a high temperature, have been confirmed. They also sought to find if the hormone on account of its action on the female genitals influenced the growth of the young animal. No action could be determined. Also Prolan can not change the blood sugar of rabbits. It is assumed, therefore, that the hormone known as Prolan excreted in the urine during pregnancy is an active endocrine function of the anterior lobe pituitary acting on the sex organs but having no effect on growth and metabolism.—J. Gagnon.

Basal gaseous metabolism of giant rats. Lee, M. O., H. M. Teel and J. Gagnon, Proc. Soc. Exper. Biol. & Med. **27:** 23. 1929.

Basal gaseous metabolism determinations were made in four giant rats which had received for four months extracts of fresh beef anterior lobe containing the growth-promoting principle. The basal metabolic rate in these animals averaged 12% less than that of their normal controls. Three weeks after the cessation of administration of the extracts, the basal metabolic rate had risen to approximately the level of the controls.—M. O. L.

Action of various pituitary extracts on the effects of insulin (Action des diverses substances hypophysaires sur l'effet de l'insuline). Magenta, M. A.

Action of extracts from the posterior lobe of the hypophysis on the sensitiveness of hypophysectomized dogs to insulin (Action des substances rétro-pituitaires sur la sensibilité a l'insuline des Chiens privés d'hypophyse). Houssay, B. A. and M. A. Magenta, Compt. rend. Soc. de biol. **102:** 428-429. 1929.

In dogs a sufficient dose of ocytocin reduces the hypoglycemic action of insulin, while vasopressin has no such effect. Hypophysectomized dogs go into convulsions after smaller doses of insulin than do normals. Ocytocin is very much more effective in relieving such animals than vasopressin.—J. C. D.

Hypophyseal dwarfishness (Hypophysärer Zwergwuchs). Lucke, H., Ztschr. f. Konstit. **14**: 430. 1929.

A description is given of a 12½-year-old girl with the development of about a 6-year-old child. During the next 2½ years she was treated with "Präphyson" tablets. Each tablet contains .3 g. dry pars anterior of hypophysis and corresponds to 1.8 g. fresh gland tissue. Three tablets were given per os for 1½ years and then 2 tablets per day the last year. During these 2½ years she grew 28 cm. in height and reached the proportions of a normal 12-year-old girl.—A. T. R.

The effect of anterior pituitary preparations administered during dietary anoestrus. Marrian, G. F. and A. S. Parkes, Proc. Roy. Soc., S. B. **105**: 248. 1929.

Anoestrus in rats was induced by a vitamin B deficient diet. The anoestrus period commences at the beginning of loss of body weight. Refeeding with a complete diet caused a return of oestrus. The administration of whole pituitary glands from rats caused the onset of oestrus in 2-3 days. This stimulation of the degenerating ovary is due to the stimulation of the large number of small follicles which are not affected by dietary deficiency. The ovary stimulating substance is present in normal amounts in the anterior pituitary glands of males on a diet deficient in vitamin B.—E. L.

Effects of transplanting anterior lobe of the hypophysis from frogs into young mice (Sur les effets de l'implantation du lobe antérieus de l'hypophyse de Grenouilles chez les Souris infantiles). Martins, T., Compt. rend. Soc. de biol. **101**: 957. 1929.

Such transplants have no effect on the growth rate of the genital tract in mice.—J. C. D.

The "all or none" law for the testicle and the hormones of the anterior lobe of the hypophysis (La loi du "Tout ou Rien" du testicle et les hormones du lobe antérieur de l'hypophyse). Martins, T., Compt. rend. Soc. de biol. **102**: 483. 1929.

Injections and implantations of anterior lobe or its hormone over a period up to ninety days failed to produce hypertrophy in the testes or genital tracts of white mice.—J. C. D.

The effects of the ocytocic and hypertensive principles (hormones) from the posterior lobe of the pituitary gland on basal metabolism (L'effet des principes (hormones) ocytocique et hypertenseur du lobe postérieur du corps pituitaire sur le métabolisme basal). Nitzescu, I. I. and J. Gavrila, Compt. rend Soc. de biol. **102**: 184. 1929.

By testing these substances on eight normal persons, it was shown that the hypertensive substance produced the rise in basal metabolism, which is usually seen after injections of posterior lobe extract.—J. C. D.

Hereditary microcephaly. Acromicria and the adipose-genital syndrome (Microcephalie familiale. Acromicrie ed syndrome adipeux-genital). Parhon, C. T. L. Ballif and N. Lawrence, Rev. franç. d'endocrinol. **7**: 308. 1929.

The authors report the cases of a microcephalic brother and sister, whose paternal aunt was also microcephalic. The condition is thought to be hereditary. Microcephaly is a symptom of acromicria as opposed to acromegaly. The boy showed marked adiposity and double cryptorchidism.—B. C.

Anterior lobe, the thyroid stimulator. V. Basal metabolism. Schwartzbach, S. S. and E. Uhlenhuth, Proc. Soc. Exper. Biol. & Med. **26**: 389. 1929.

The effect of several preparations of the anterior and posterior lobe of the hypophysis on the metabolism of ambystoma larvae was studied by Winkler tests. Larvae of two species were used, unanesthetized and in chloretone

anesthesia. Feeding of either anterior or posterior lobe preparations was without effect on the metabolism. Intraperitoneal injections of an extract of beef anterior lobe caused a 30 to 50% increase in the average oxygen consumption of unanesthetized larvae and a 114% increase in anesthetized larvae.
—M. O. L.

The oxytocic substance of cerebrospinal fluid. Van Dyke, H. B., P. Bailey and P. C. Bucy, J. Pharmacol. & Exper. Therap. **36**: 595. 1929.

The oxytocic substance of cerebrospinal fluid appears to be calcium. Reduction of the calcium to a concentration equalling that of an artificial "cerebrospinal fluid" bathing the isolated uterus abolishes the oxytocic action and yet causes no destruction or removal of true posterior-lobe oxytocic principle. Properly preserved human ventricular and lumbar fluids of normal calcium concentration have an oxytocic effect. The melanophore-expanding effect of cerebrospinal fluid and serum may be due to differences between their calcium concentrations and those of artificial fluids used in the limb-perfusion method of assay.—Authors' Summary.

Liver and thyroid: Hyperfunction of the liver in Basedow's disease (Leber und Schilddrüse: Die Hyperfunktion der Leber bei Basedowkranken). Pende, N., Endokrinol. **1**: 161. 1928.

On the basis that certain functional tests give opposite results in Basedow's disease and cases of known hepatic deficiency, Pende concludes that the liver produces a hormone that is synergistic with that of the thyroid. Hyperthyroidism results in an excess of this liver hormone. This conclusion is supported by the observation of excessive bile secretion in hyperthyroidism. Various theoretical corrolaries of this conception are outlined.—R. G. H.

Can the islets of Langerhans transform themselves into acinar tissue? (Les ilots de Langerhans font-ils retour aux acini?). Bierry, H. and M. Kollman, Compt. rend Soc. de biol. **101**: 17. 1929.

Frogs, marmotts, and pigeons were examined during periods favorable to such a change, when the acinar tissue was increasing rapidly, as after hibernation. There was no indication of islet tissue altering to form acinar cells.
—J. C. D.

Dextrose insuline equilibrium (L'equilibre dextrose-insuline). Bouckaert, J. P., P. Denayer and R. Krekels, Compt. rend. Soc. de biol. **101**: 511. 1929.

Two tables are given showing the amounts of glucose necessary to balance a given dose of insulin in normal rabbits.—J. C. D.

Glucose-insulin equilibrium (Équilibre glucose-insuline). Bouckaert, J. P., P. De Nayer and R. C. Kerekels, Arch. internat. de physiol. **31**: 180. 1929.

Glucose solution, rendered isotonic with sodium chloride, was injected from a burrette-like apparatus into one of the ear veins of an immobilized rabbit. The other ear was used for injecting insulin and drawing blood. By varying the amounts of insulin and glucose injected, the authors determined the following relationships: The maximum amount of glucose per hour which can be caused to disappear by insulin injection into a rabbit is 1.26 gram per kgm. of body weight. The maximum quantity of insulin which can be utilized by the rabbit for glucose destruction per kgm. of body weight is 6.8 units. Amounts of insulin above this are inactive.—E. L.

The physiological significance of the primary insulin hyperglycemia (Die physiologische Bedeutind der primären Insulinhyperglykämie). Bürger, M., Am. J. Physiol. **90**: 302. 1929.

Intravenous injection of insulin has as a consequence a temporary increase of the blood sugar in man and in animals. The degree of blood sugar increase is dependent upon the vascular region in which the insulin injection takes place, upon the size of the insulin dose, and upon the glycogen content of the liver. In man an average increase of 20 per cent in blood sugar appears 5 to

10 minutes after the intravenous injection of ½ unit of insulin per kgm. body weight. With corpulent people and myxedematous patients the blood sugar may rise 50 per cent over the initial value under similar conditions. After direct injection of 1-2 units of insulin into the portal vein or one of its branches the increase of blood sugar averaged 35.3 per cent in 21 tests on dogs. If the insulin is injected in the jugular vein and the circulation of blood in the liver is stopped by ligation of the liver hilus the increase of blood sugar in the peripheral blood does not take place. The initial hyperglycemia after insulin injection is thus probably due to the discharge of glycogen from the liver. This thesis is proven by glycogen determinations made at consecutive 10-minute intervals upon the dog's liver by means of a special method. The liver after insulin injection in the portal vein regularly becomes poorer in glycogen. This loss of glycogen becomes the greater, the higher the blood sugar value rises after insulin injection. For example, the loss can amount to as much as 50 per cent of the initial value by injecting 2 units of insulin per kgm. of body weight into a 17.5 kgm. dog. The absolute glycogen loss becomes greater, the higher the initial value of the liver glycogen.—J. Gagnon.

Influence of insulin on the oestrous cycle in the white rat (Action de l'insuline sur le cycle oestral du Rat blanc). del Castillo, E. B. and C. Calatroni, Compt. rend. Soc. de biol. **102**: 454. 1929.

In eight animals, daily injections of insulin over varying periods had no demonstrable influence on the cycle.—J. C. D.

The insulin fattening cure in pulmonary tuberculosis (La cure insulinique d'engraissement dans la tuberculose pulmonaire). Combemale, F., C. Gernez and A. Breton, Ann. de med. **26**: 480. 1929.

The optimum dosage of insulin was 30 units per day administered in two injections. The administration of 45-60 units was deleterious. The 32 cases which were treated by this method of fattening always showed an amelioration of the symptoms coincident with the increase in weight. The authors feel that the results of this method are truly remarkable.—E. L.

Further observations on latent tolerance in diabetics. Gibson, R. B., Proc. Soc. Exper. Biol. & Med. 26: **449.** 1929.

Three diabetic patients under insulin treatment were given high sugar diets. The insulin dosage was gradually reduced and finally stopped. One patient was continued 40 days on the high carbohydrate diet without insulin. In the other two cases insulin had to be resorted to again after about two weeks, but there was an increased hypoglycemic response to small doses.
—M. O. L.

Death of a totally depancreatized dog treated with insulin for 57 months (Mort d'un Chien totalement dépancréaté traité par l'insuline pendant 57 mois). Hédon, E., Compt. rend. Soc. de biol. **100**: 698. 1929.

This dog of about 7 kgm. weight received daily two subcutaneous injections of insulin and a general diet, meat, bread, milk and sugar up to 500 calories. He remained in good health under these conditions, but there was no evidence of better utilization of carbohydrates. For several months before death, larger doses of insulin were necessary. The dog died in convulsions probably due to hypoglycemia. Marked emaciation, fatty degeneration of the epithelial cells of the kidney tubules, and a thickening of the adventitia of the blood vessels generally, were the only pathological changes found.—J. C. D.

Insulin and CO_2 combining power of blood plasma in normal dogs. Hill, R. M. and W. B. Draper, Proc. Soc. Exper. Biol. & Med. **27**: 31. 1929.

In four normal dogs after the subcutaneous administration of insulin there was within 40-50 minutes a slight rise in the CO_2 combining power of the blood plasma, followed by a pronounced fall to a level considerably lower than the initial. The authors consider that the results indicated that insulin may intensify a non-ketogenic acidosis. The dosage of insulin used in the experiments was 2 or more units per kilogram.—M. O. L.

Effect of insulin with simultaneous administration of cyanide (Beiträge zur Wirkung des Insulins bei gleichzeitiger Anwendung von Blausäure). Hosoda, N., J. Biochem. **10**: 383. 1929.

Sublethal injections of cyanide induce hyperglycemia in rabbits, which can be controlled by insulin. This is evidence that insulin is not the activator of hexose-diphosphate formation.—B. S. Walker.

Results of continuous insulin injections in depancreatized dogs (Effet des injections continues d'insuline chez le Chien dépancréaté). Houssay, B. A., J. T. Lewis, V. G. Foglia, Compt. rend. Soc. de biol. **101**: 241. 1929.

A continuous injection of about one one-hundredth unit of insulin per kgm. per hour serves to keep the blood sugar of a depancreatized dog normal. —J. C. D.

Pancreas and blood sugar regulation (Papel de pancreas en la regulacion de la glucemia 2aCom). Houssay, B. A., J. T. Lewis and V. G. Foglia. Rev. Soc. Argent. Biol. **5**: 1. 1929. Abst., Physiol. Absts. **14**: 446.

Insulin was injected intravenously into dogs, (a) normal, (b) pancreatectomised, (c) pancreatectomised with a pancreas grafted in the carotid artery and jugular vein. The drop in blood sugar was similar in the 3 series of experiments. The recovery was slightly more rapid in series (b) than in series (a). In series (c) the recovery was much slower. This is taken as proof of the existence of inhibitory fibres in the extrinsic innervation of the pancreas. In their absence, the pancreatic graft continues secreting insulin in spite of the low blood sugar level, and so hypoglycemia is prolonged, whilst in the normal dogs the recovery is prompter because the insulin secretion is inhibited when the blood sugar falls.

Endocrine function of normal and denervated pancreas during insulin hypoglycemia (La fonction endocrine du pancréas normal ou énervé pendant l'hypoglycémie insulinique). Houssay, B. A., J. T. Lewis and V. G. Foglia. Compt. rend. Soc. de biol. **101**: 239. 1929.

Dogs with pancreatic grafts to replace the extirpated pancreas recovered from the hypoglycemia more slowly than controls. This slow return of blood sugar to normal is due to a retarded response of the graft, which continues secreting an excess of insulin for a longer period than if it had its proper nerve supply.—J. C. D.

The initial hyperglycemic influence of insulin (Action hyperglycémiante initiale de l'insuline).

On the mechanism producing the early hyperglycemia following insulin (Sur le mecanisme de l'hyperglycémie initiale provoquée par l'insuline). Ionesco, D., I. Cosmulesco and M. Tomesco, Compt. rend. Soc. de biol. **102**: 167, 170. 1929.

This short initial phase was found in dogs, rabbits, and man following intravenous administration. This increase in blood sugar is at a maximum 5 to 13 minutes after injection and varies from 8 per cent seen in a man to 137 per cent seen in a dog. This peak is followed at once by a steady and rapid decline. This rise is dependent on glycogen in the liver, since diabetics with glycogen poor livers do not give it. Paralyzing the sympathetics of the liver in dogs, either by cutting or drugs, does not eliminate the increase in blood sugar, so the action of the insulin must be a direct hormonal one on the liver cells.—J. C. D.

Physiological studies on insulin. Memoir I.—Rapid disappearance of insulin injected into the blood stream (Études physiologiques sur l'insuline. I er memoire.—Rapide disparition de l'insuline injectée dans le torrent circulatoire). Képinov, L. and S. Petit-Dutaillis, Arch. internat. de physiol. **31**: 310. 1929.

The dogs used were anesthetized with chloralose. The carotid artery and jugular vein of the donor and recipient were anastomosed. Insulin (10-30 units) was injected intravenously. Transfusions of blood (180 cc.-1160 cc.)

from donor to recipient were made immediately, 3, 8 and 25 minutes after the injection of insulin. The blood sugar of the donor was always reduced whereas the recipient receiving a transfusion 25 minutes after the insulin injection, maintained a constant blood sugar. The same was true when the transfusion was made after 8 minutes. When the transfusion of small amounts of blood (less than 500 cc.) was made after three minutes there was only a slight diminution in the blood sugar of the recipient. When the amounts of the transfusions were large (about 1000 cc.) there was a lowering of the blood sugar of the recipient. When the transfusion was made immediately after the injection of insulin, the blood sugar of the recipient was markedly lowered. After partial removal of the liver from the circulation of the donor, the transfused blood of the donor which had received insulin 20 minutes previously would still cause a lowering of the blood sugar of the recipient. The authors believe that the liver plays an important part in the fixation of insulin by the tissues.—E. L.

Pathogenesis of diabetes mellitus of pancreatic origin. Mauriac, P. and E. Aubertain, Paris méd. **1**: 440. 1929. Abst., J. A. M. A. **93**: 242. 1929.

Mauriac and Aubertin discuss the complexity of the pathogenesis of diabetes mellitus and, leaving aside the rôle of disturbance of various endocrine glands (such as the thyroid, suprarenals and hypophysis), the nervous system and the liver, try to explain the mechanism involved in the pathogenesis of diabetes mellitus of pancreatic origin. Placing insulin in contact with the whole blood, blood serum, plasma or erythrocytes of healthy and sick persons, respectively, they observed an inactivating effect of these substances on the insulin. The same results were observed in experiments with extracts of various organs, such as muscles, kidneys or lungs. The inactivation of insulin was greater by the blood of patients with diabetes mellitus and was maximal in the presence of hemolyzed erythrocytes. This was explained by the presence in the erythrocytes of some substance having the power to neutralize insulin. If the permeability of the membrane of the erythrocytes is abnormally increased, this neutralizing substance may inactivate the insulin secreted by a normal pancreas and thus cause hyperglycemia, or the combination of decreased pancreatic secretion and of neutralization of insulin may be present. Only rarely are the pathologic changes in the pancreas so advanced as to explain diabetes mellitus by a deficiency of the pancreatic secretion only.

Notes on a dog kept alive by insulin for fifteen months following removal of pancreas sur un chien dépancréaté maintenu en vie pendant 15 mois par l'insuline). Mauriac, P. and E. Aubertin, Compt. rend. Soc. de biol. **101**: 52. 1929.

The animal was maintained by replacing the external secretion of the pancreas by feeding pancreatin, and replacing the internal secretion by insulin.
—J. C. D.

The lipoid splitting action of lungs in life as related to the internal secretion of the pancreas (La lipodiérèse pulmonaire in vivo et la sécrétion interne du pancréas).

The lipoid splitting action of the lungs in vitro and the internal secretion of the pancreas (La lipodiérèse pulmonaire in vitro et la sécrétion interne du pancréase). Nitzescu, I. and G. Benetato, Compt. rend. Soc. de biol. **101**: 71. 1929.

In normal dogs there is a decrease of about 9 per cent in the fats and cholesterol during the passage of the blood through the lungs. This decrease falls to about one-tenth its normal value after removal of the pancreas. A nearly normal decrease takes place, however, if the animals are treated with insulin. The same relations hold in breaking down of fats by pieces of lung in vitro. Lungs from depancreatized dogs show a diminution of this power which cannot be restored by mixing insulin with the excised lung, but which reaches nearly normal figures if the dogs have been treated with insulin previous to the excision of the lung tissue.—J. C. D.

The reaction of the saliva and its resistance to change of reaction in experimental diabetes—effect of insulin (Réaction actuelle et potentielle de la salive dans le diabète expérimental.—Action de l'insuline). Peluffo, A., Compt. rend Soc. de biol. **102**: 468. 1929.

In sixteen diabetic dogs, the pH of the saliva was not much altered, nor was the pH affected by insulin. The alkali reserve was not altered regularly in diabetes, but was increased by insulin.—J. C. D.

Studies on the cardiovascular effects of insulin. Räihä, C. E., Skandin. Arch f. Physiol. **57**: 243. 1929. Abst., Chem. Absts. **23**: 4507.

Intravenous injection of insulin causes a diminution of the minute volume of the heart. This diminution continues for some time and in certain cases is followed by a transient increase. A second injection does not affect the minute volume as much as the first, and may even be without any action. The reduction in the minute volume is due to a diminution of the beat volume of the heart. The blood pressure in the aorta falls for about 10-30 minutes after an intravenous insulin injection, this fall being sometimes preceded by a brief rise in pressure. The fall in pressure is caused by the diminished minute volume and only very rarely also to vasodilation. Generally the fall in the aortic pressure is accompanied by a constriction of the vessels which may become so pronounced that it is responsible for the observed secondary rise in pressure, and this vasoconstriction is attributed to the outpouring of adrenaline under the influence of insulin. Immediately following an insulin injection, the pressure in the pulmonary artery increases, owing to a vasoconstriction. The occasional lowering of the pulmonary arterial pressure seems to be due to the adrenaline effect. Following an insulin injection, the effect of vagus stimulation on the heart is more or less reduced, but this diminution does not generally occur if adrenaline is injected before the vagus is stimulated. These cardiovascular effects of the insulin are shown to be due to changes in the K and Ca content of the circulating medium produced by the insulin.

The absorption of glucose by the blood cells from diabetic dogs (L'absorption de glucose par les hématies provenant de Chiens diabétiques).

Does there exist in diabetic plasma a substance which interferes with the absorption of glucose by the blood cells? (Existe-t-il dans le plasma diabétique une substance modifiant l'absorption globulaire du glucose?) Rathery, F., R. Kourilsky and Mlle. S. Gibert, Compt. rend. Soc. de biol. **100**: 643. 1929.

The action of the red cells toward glucose was the same whether they came from diabetic or control animals. There was no evidence that an interfering substance existed in the blood of the diabetic animals.—J. C. D.

Influence of insulin on the absorption of glucose by normal blood cells (Influence de l'insuline sur l'absorption du glucose par les hématies normales). Rathery, F., R. Kourilsky and Mlle. Yv. Laurent, Compt. rend. Soc. de biol. **100**: 726. 1929.

Centrifugal blood cells of normal dogs were treated with insulin in vitro and tested. Insulin did not influence the absorption of glucose.—J. C. D.

Influence of insulin on the absorption of glucose by red cells in diabetic dogs (Influence de l'insuline sur l'absorption globulaire du glucose chez les Chiens diabétiques). Rathery, F., R. Kourilsky and Mlle. S. Gibert, Compt. rend. Soc. de biol. **100**: 728. 1929.

Red cells tested after addition of insulin in vitro and after injection of insulin into the depancreatized dog showed no change in their absorptive power.—J. C. D.

Pruritis. Sparks, R. A., Missouri State Med, Assoc. **26**: 24. 1929.

In a number of cases of pruritis (anal, scrotal, vulval and general), whether accompanied or not with glycosuria, the administration of insulin was of marked benefit. Some of the cases were longstanding and the patients were able to obtain temporary relief only from cocaine ointment. In one case with the scrotum and penis enormously swollen and raw from scratching,

insulin relieved the itching in three days, the swelling in less than a week. In cases without glycosuria the insulin dosage was at first 2 to 10 units twice daily, then increased to 10 to 20 units twice a day.—Author's Abst.

Contribution to the study of the physiological variations of the internal secretion of the pancreas. Relation between the external and internal secretions of the pancreas (Contributions a l'étude des variations physiologiques de la sécrétion interne du pancréas. Relations entre les secretions externe et interne du pancréas). Zunz, E. and J. La Barre, Arch. internat. de physiol. **31**: 20. 1929.

The injection of secretin causes a gradual diminution of blood sugar. This decrease in blood sugar is proportional to the secretagogue action of the secretin. This increased insulin after secretin injection is not dependent on the vagus as it can be produced after section of the vagi. That this is not a direct action of the secretin on the blood sugar, but is an action on the Islands of Langerhans, was proven by transfusion experiments using the author's pancreato-jugular anastomosis technique.—E. L.

Contributions to the study of the physiological variations of the internal secretion of the pancreas. VII. The hypoinsulism following the state of hypoglycemia (Contributions a l'étude des variations physiologiques de la sécrétion interne du pancréas. VII. De l'hypoinsulinémie consecutive aux états d' hypoglycemie). Zunz, E. and J. La Barre, Arch. internat. de physiol. **31**: 162. 1929.

These authors have produced hypoglycemia by several methods, i. e., insulin, hepatectomy and synthalin. The hypoglycemia produces a decrease in insulin secretion. The diminution in insulin secretion is caused by the superior nerve centers acting by means of the vagus. The exact location of these centers is not known—E. L.

Studies on the pH and alkaline reserve in thyro-parathyroidectomized dogs (Recherches sur le pH et la réserve alcaline chez les Chiens thyro-parathyroidectomisés). Parhon, C. I., H. Derevici and M. Derevici, Compt. rend. Soc. de biol. **101**: 613. 1929.

The authors found no change in the pH, but a diminution in the alkaline reserve.—J. C. D.

Parathyroid tumor and skeletal abnormalities. Snapper, I., Nederl. Tijdschr. v. Geneesk. **73**: 4758. 1929. Abst., J. A. M. A. **93**: 1851.

Snapper reports that in a man, aged 56, who was affected with marked decalcification of the bones, associated with severe pains, particularly in the legs and knees, it was found that the disease had begun as generalized osteitis fibrosa cystica. There was a pseudo-osteomalacic end-stage resembling that of Recklinghausen's disease. The calcium content of the blood serum was much increased, which was interpreted as an expression of an overactive parathyroid. There was a small tumor in the thyroid. A tumor in one of the parathyroids was suspected and was found at operation. After extirpation of this small tumor, a decided improvement in the patient's condition was noted.

The presence of histamine and acetyl-choline in the spleen of the ox and the horse. Dale, H. H. and H. W. Dudley, J. Physiol. **68**: 97. 1929.

A method is described by means of which a substance identified as histamine was isolated from the spleen, also a substance identified as acetylcholine, demonstrating the natural occurrence of the latter in animal tissues. This substance reproduces the effects of true parasympathetic stimulation. It has not been found in the spleen of the dog, cat, monkey or rabbit.—C. I. R.

Experiments on the Bartonella infection in the white rat (Experimentelle Untersuchungen uber Bartonella-Infection der Weissen Ratten). Friedberg, S., Endokrinol. **3**: 84. 1929.

Rats from Switzerland, Hamburg, Vienna and Berlin show 100% cases of Bartonella and anemia after spleenectomy with death in about 30% of the cases. Two Italian rats did not show any infection after spleenectomy. One

of these was caused to have the disease by blood transfusion from an infected animal. The author believes therefore that he is dealing with an infectious disease. Bartonella infection, unaccompanied by anemia, can be produced by blocking the reticulo-endothelial system in a normal rat with ferric lactate or India ink. This block, if produced after spleenectomy, results in a typical Bartonella-anemic symptoms. He concludes that the spleen, through an unknown factor, plays a defensive rôle.—B. C.

Origin of Hassall's corpuscles (Über die Entstehung der Hassalschen Körperchen). Juba, A. and P. V. Mihalik, Ztschr. f. Anat. u. Entwcklngsg. **90:** 278. 1929.

As a result of a histological study of two human foetuses and one newborn and numerous pig foetuses, the authors conclude that Hassall's corpuscles arise by enlargement of reticular cells followed by degeneration of the centrally located cells. Eight good illustrations.—A. T. R.

Studies on the action of thyroxin on heat regulation (Studien über die Wirkung des Thyroxins auf den tierischen Organismus und imbesondere auf die Wärmeregulation des Gleichwarmblüters). Abderhalden, E. and E. Wertheimer, Arch. f. d. ges. Physiol. **219:** 588. 1928.

Rats and mice are much more resistant to thyroxin than dogs, rabbits and guinea pigs. Rats given thyroxin are more sensitive to increased environmental temperature than normals and show a quicker exhaustion of the glycogen store of the liver. There is a lowering of the blood sugar and an increased CO_2 production.—M. O. L.

Studies on the effects of thyroid glands from normal and treated rabbits on the growth of epithelioma in white mice (Recherches sur l'action du corps thyroïde du Lapin normal ou préparé sur l'évolution de l'épithélioma expérimental de la Souris blanche). Arloing, F., A. Josserand and J. Charachon, Compt. rend. Soc. de biol. **100:** 665. 1929.

Bits of thyroid, both from normal rabbits and from ones which had received previous injections of a suspension of the tumor, were transplanted into mice. Neither type of graft had any effect on the growth of the tumor in the mice.—J. C. D.

The interrelation of the thyroid and the other organs (Die Beziehungen der Schilddrüse zu Funktionsgebieten anderer Organe). Asher, L., Schweiz. med. Wchnschr. S. 802. 1927.

The interrelation between the system thyroid-spleen-bone marrow was shown by two series of experiments. Normal rabbits regenerate blood rapidly if Loewys Hämatopoetines are injected. After extirpation of the thyroid the animals did not react towards the same dose of hämatopoetines, but the reaction returned after extirpation of the spleen. Injection of nucleic acid causes hyperleucocytosis in normal rabbits and a characteristic histological picture of the bone marrow. Both reactions of nucleic acid injection disappear after extirpation of the thyroid gland. Again both reactions reappear after the spleen too has been extirpated. Extirpation of the spleen increases the water metabolism of guinea-pigs; thereupon extirpation of the thyroid lowers the level of water metabolism. These facts show antagonistic regulation of water metabolism by thyroid and spleen. The increase of basal metabolism by adrenalin is markedly diminished after extirpation of the thyroid in rats.
—Author's Abst.

Effects of thyro-parathyroidectomy on the excitability of the great splanchnic nerve in the dog (Influence de l'ablation des thyroïdes et des parathyroïdes sur l'excitabilité du nerf grand splanchnique chez le Chien). Chauchard, A., B. Chauchard and E. Czarnecki, Compt. rend. Soc. de biol. **100:** 1114. 1929.

This operation affects the response of the organs innervated but not the conducting powers of the nerve.—J. C. D.

The thyroid problem (Das Thyreoideaproblem). Boothby, W. M., Endokrinol. **3:** 1. 1929.

A general article setting forth particularly the work of the Mayo Clinic and notable for an excellent and extensive bibliography.—R. G. H.

Experimental hyperthyroidism and sympathetic irritability. Chamberlain, Beulah, Proc. Soc. Exper. Biol. & Med. **26**: 459. 1929.

Dogs fed disiccated thyroid substance showed no greater increase in the blood pressure response to adrenin than did normal dogs.—M. O. L.

The importance of carbohydrate metabolism in hyperthyroidism.—Charvát, J., Otolaryngologia Slavica, **1**: 2. 1929.

From several years of clinical investigation the author concludes that there exists no direct antagonism between the thyroid and the pancreas. One cannot say that in hyperthyroidism the endocrine function of the pancreas is checked by the increased activity of the thyroid. The liver of hyperthyroid individuals is labile, owing to the increased sympathetic tonus. It is not able to fix well the administered sugar, and instantly hands it over to the blood. The liver is, therefore, poor in glycogen, and after a sugar test meal the blood-sugar rises above the physiological level. The kidney-sugar threshold rises in a compensatory manner, so that loss of sugar is prevented thereby, and glycosuria appears in only one-fifth of the cases. Sugar is a well-utilizable and necessary matter for hyperthyroid organisms, because it covers very quickly the energetic needs of the tissues, due to an increased basal metabolism. Oxidation of the sugar is higher in hyperthyroidism than in normal conditions, while the storage of glycogen is weaker, its synthesis being inadequate. The autonomous fixation of the sugar by the tissues (without direct influence of insulin) is very active. As soon as the immediate energetic need in the tissues is satisfied, the sugar remaining uselessly in the tissues can flow over into the venous blood and urine, without having been polymerised into glycogen. If glycosuria appears, it is generally of small extent and shows no tendency to develop into true diabetes. If a disproportion of insulin production and carbohydrate plethora takes place, it signifies a relative and functional disturbance only, which can be repaired by the systematic education of the pancreas to a greater internal function. Administration of small doses of insulin is also able to ameliorate this stage. The functional efficacy of the liver in hyperthyroidism is lowered, owing to the lack of glycogen stores. It is necessary to pay attention to this fact in all operative interventions.—R. G. H.

Cancer of the thyroid gland. Clute, H. M. and L. W. Smith, Arch. Surg. **18**: 1. 1929.

The incidence of cancer of the thyroid in 3,389 operative cases in the Lahey clinic was 1.68 per cent. There were 6.4 times as many women as men who had malignant disease of the thyroid. The greatest incidence of the disease was between the ages of 50 and 65. Cases occurred in persons aged 20 and 82. An adenomatous goiter preceded the malignant disease in 94.4 per cent of the cases studied. Histologically, cancer of the thyroid may be divided in to four chief groups: (1) Malignant adenoma; (2) squamous cell carcinoma; (3) giant cell carcinoma, and (4) small cell carcinoma. Cases in each of these groups have a marked similarity in their clinical history and course. Knowledge of the histoloical group of a cancer of the thyroid gives valuable information as to (a) the chances of recovery of the patient, or (b) the probable duration of life, and (c) the advisability of roentgen treatments. When cancer of the thyroid can be diagnosed clinically, the chances of cure are small. Lowering the mortality of thyroid malignant disease must at present depend on the removal of the premalignant adenoma. Surgical removal and postoperative roentgen treatment give some good results in the first histologic group (malignant adenoma). Treatment has not been of any real value in the other types of malignant disease of the thyroid.—Authors' Abst.

The passage of the maternal thyroid hormone through the placenta to the fetus (Sur le passage de l'hormone thyroïdienne de la mère au fetus a travers le placenta). Courrier, R. and M. Aron, Compt. rend. Soc. de biol. **100**: 839. 1929.

Pregnant dogs were fed an excess of beef thyroid. Their thyroids showed the histological signs of atrophy. The glands of the pups were normal. If the thyroid feeding to the mothers was continued so that there was an excess of

thyroid hormone in the milk, the glands in the pups atrophied. The placenta then prevented the fetus from receiving an excess of thyroid from the mother, i. e., it is not permeable to the thyroid hormone.—J. C. D.

Tissue respiration and endocrine functions, III. Influence of thyroidectomy on tissue respiration. Dye, J. A. and G. H. Maughan, Proc. Soc. Exper. Biol. & Med. **26**: 439. 1929.

Dogs were thyroidectomized when 5 weeks of age. Seven months later the oxygen consumption of finely minced skeletal muscle of the "cretin" pups was 25 to 60 per cent less than that of muscle from normal litter mates of the same sex. The authors adhere to the view that the thyroid hormone exerts an influence upon the oxidative system of body cells.—M. O. L.

Tissue respiration and endocrine function. IV. Influence of thyroidectomy on succinoxidase activity of surviving tissues. Dye, J. A. and G. H. Maughan, Proc. Soc. Exper. Biol. & Med. **26**: 441. 1929.

Muscle tissue from thyroidectomized pups showed a diminution of 16 per cent as compared with normal controls in the power to oxidize succinic acid.
—M. O. L.

Occurrence of asthma in patients manifesting evidences of thyroid dysfunction. Elliott, C. A., Am. J. Surg. **7**: 33. 1929.

The coincidence of asthma with hypothyroidism in one case and hyperthyroidism in 5 cases is reported. The clinical observations suggest, but do not demonstrate, in the author's opinion, that a physiological relationship may exist between asthma and hyperthyroidism. Their coexistence may be merely casual. The fact that but 6 patients thus afflicted have been seen in this clinic during the past 11 years would tend to support the latter view. Since 2 of these patients have been definitely relieved of asthma and hyperthyroidism by thyroidectomy and clearing up of definite focal infections, such a procedure seems warranted as a method of treatment. Adrenalin relieved 4 temporarily of asthma while hyperthyroid, although one had a frightful general reaction. Adrenalin relieved 2 of asthmatic attacks during periods in which they were definitely hypothyroid. Iodine had a beneficial effect on the asthma in one patient who was continuously hypothyroid, but no conclusion can be drawn as to the effect of the iodine alone on the asthma of the others, although it was given to all of them, and the thyroid status of 4, while definitely hyperthyroid, seemed improved thereby.—R. G. H.

Quantitative observations on thyroxine and allied substances. II. Effects on the oxygen consumption of rats. Gaddum, J. H., J. Physiol. **68**: 383. 1930.

The technique is described in detail. Mean consumption was 14.44 cc. 0_2 per kgm. per min. (.00700 cal. per sq. m. per 24 hrs.). The most effective method of administration of thyroxin was found to be subcutaneous injection of alkaline water solution. The response was decreased after thyroidectomy and increased after a previous injection, l-thyroxin being more effective than d-thyroxin. Thyreoglobulin was more effective than thyroxin when given orally. Subcutaneous injection gave responses proportional to the respective iodine contents. Two dipeptids containing thyroxin, n-acetylthyroxin, l-acetylthyroxin, diiodothyronine were all effective. Replacement of the iodine with bromine gave a substance slightly effective. Thyronine, thyroxamine, diiodotyrosine and B-dialanine were ineffective.—C. I. R.

Thyrotoxicosis in childhood. Ginsburg, S., Am. J. Dis. Child. **37**: 922. 1929.

This condition is not as rare in children as formerly supposed, and while its course is milder and more atypical than in the adult, it may run an acute course with a fatal termination. The paper is a plea for the use of radium in preference to surgical intervention in toxic goiter. In the differentiation between the simple and toxic types of goiter, the author employs two tests: the iodine and radium therapeutic tests. Iodine either ameliorates or aggravates the symptoms of exophthalmic goiter or of toxic adenoma, but it rarely affects simple goiter. In the latter type, there is rarely any constitutional effect, even

with marked shrinkage of the thyroid gland. The application of radium is followed by an improvement in toxic cases, but not in simple goiter, asthenia or neuro-circulatory conditions.—M. B. G.

Influence of the thyroid on blockage of the reticulo-endothelial system (Influence de la thyroïde sur le blocage du système réticulo-endothélial).

A new method for measuring the activity of thyroid preparations (Nauveau mode de détermination des préparations thyroidiennes). Goebel, F., Compt. rend. Soc. de biol. **101**: 596. 1929.

In normal dogs injections of colloidal silver, in sufficient amounts to cause blockage of the endothelial system, produces a hypoglycemia and a reduction in cholesterine. In thyroidless dogs injections of silver cause no such reduction. Thyroidless dogs fed thyroid for a period respond as do normal dogs. This result of thyroidectomy may be due to (1) a reduction in the phagocytic activity of the endothelium, (2) a reduction in the tonus of the sympathetic system, or (3) increased glycogen fixation in the liver. The activity of thyroid preparations may be gauged by testing their ability to restore the normal blocking and resultant hypoglycemia in thyroidless dogs.—J. C. D.

Effect of feeding small doses of potassium iodide on the thyroid gland. Gray, S. H. and J. Rabinovitch, Proc. Soc. Exper. Biol. & Med. **26**: 468. 1929.

The daily feeding of 0.0001 gm. KI to guinea pigs did not increase the number of mitoses and did not affect the structure of the thyroid gland. Feeding daily 0.0001 gm. KI to guinea pigs produced only a slight increase in mitoses, but at the same time produced an otherwise histologically active thyroid gland. The feeding of 0.01 gm. KI stimulated the thyroid in all its histological phases.—M. O. L.

Pathogenic basis for iodine treatment in thyrotoxicosis. Holst, J., Norsk. Mag. of Laegevidensk. **90**: 973. 1929. Abst., J. A. M. A. **93**: 1516.

Holst treats of the action of iodine in primary thyrotoxicosis (exophthalmic goiter) and considers the changes in the blood and goiter produced by the iodine treatment of thyrotoxicosis according to Plummer. The thyroid has two functions, as follows: (1) the production of the secretion and (2) the storage of the secretion and the regulation of its discharge. Administration of inorganic iodine is believed to arrest the "thyroid diarrhea" or rapid discharge of the thyroid secretion into the blood in thyrotoxicosis. The relation between the inorganic iodine in the blood and the capacity of the thyroid to retain its secretion, called the "intermediary iodine balance," is discussed.

Effect of thyroid administration on protein and fat metabolism (Über den Einfluss von Schilddrüsendarreichung auf den Eiweiss- und Fettstoffwechsel). Kommerell, B., Biochem. Ztschr. **208**: 112. 1929.

A dog was subjected to a fasting period of 18 days, a rest period of five weeks, and then another fasting period of 17 days. During the second fast period thyroid (5 grams Gland. thyr. Merck) was given daily. Daily studies were made during both periods of the nitrogenous equilibrium and of the basal metabolism. From these data the percentages of protein and fat consumed were calculated. Thyroid administration led to an increase of 30.5% in the basal metabolic rate, 31.3% of which was attributed to the combustion of protein, 68.7% to the combustion of fat: the nitrogen output was doubled. Complete tables and graphs are given, as well as description of some modifications of the Haldane gas analytical method.—B. S. Walker.

Action of the thyroid gland on proteins (La fonction protéocrasique du corps thyroïde). Loeper, M., A. Lemaire and J. Tonnet, Compt. rend. Soc. de biol. **102**: 279. 1929.

Blood in the thyroid arteries and veins of dogs and horses was studied. The nucleo albumin was much decreased, the serine increased, the sulphur left after precipitation of the albumins was increased, and the amino acids reduced by passage of the blood through the gland. The total blood albumin remained unchanged. Similar results followed when thyroid extract was added to blood in vitro.—J. C. D.

Experimental researches on heredity of thyroid conditions (Recherces expérimentales sur l'hérédité thyroïdienne). Marza-Rusnac, E., Rev. franç. d'endocrinol. **7**: 320. 1929.

In guinea pigs thyroidectomy of the parents results in a lessening of the size and weight of the thyroid of the new born. The offspring of hyperthyroidised animals are weaklings, whose weight at birth is less than that of controls.—J. Gagnon.

The sedimentation velocity of erythrocytes in thyrotoxicosis. Mora, J. M. and J. T. Gault, J. Lab. & Clin. Med. **15**: 590. 1930.

The sedimentation speed of erythrocytes was studied in 30 cases of thyrotoxicosis, by the Linzenmeier method, before and after thyroidectomy. The rate was increased in all cases before operation. The administration of iodine decreased the speed of sedimentation in 6 out of 11 cases, and increased it in 5 cases. Thyroidectomy was followed by an increased rate in 13 cases, and by a decreased speed in 14 cases. There seemed to be little parallelism between the sedimentation velocity, the basal metabolic rate, and the clinical picture.—Authors' Summary.

Studies on the behavior of cholesterol within the animal body. IV. The rôle of thyroid gland in the content of cholesterol in each organ and tissue. Onizawa, J., J. Biochem. **10**: 425. 1929.

Analysis was made of tissues for free and ester cholesterol in rabbits with thyroids removed, similar animals with adrenalin injection; also in animals fed thyroid, and the same plus adrenalin injection. Full results are given in tabular form. Following thyroid removal, ester cholesterol is increased in plasma and adrenals. Adrenalin injections lead to an increase in free cholesterol in the tissues, whether or not thyroid be present.—B. S. Walker.

An inquiry into the fate of thyroxin in the treatment of nephrosis. Platt, R., Quart. J. Med. **23**: 129. 1929.

Patients with chronic nephrosis have an extraordinary tolerance to thyroxine given either orally or intravenously. This is not due to rapid excretion of thyroxin by the kidney. It is therefore presumed that thyroxin is either rapidly destroyed in the body, or its action inhibited, but it is suggested that such an inhibition does not depend upon the increased level of the blood cholesterol which is commonly found in these cases.—E. C. Kendall.

Effect of infections on the thyroid gland. Rabinovitch, J and S. H. Gray, Proc. Soc. Exper. Biol. & Med. **26**: 472. 1929.

In 22 guinea pigs an acute and chronic peritonitis was induced by injecting fecal material intraperitoneally. In only one guinea pig examined before death was any desquamation of epithelium and softening of the colloid in the thyroid gland noted. In guinea pigs found dead, post mortem desquamation occurred earlier in experimental infections than in controls. In chronic infections, the guinea pig thyroid presented no deviations from the normal.—M. O. L.

The thyroid gland of sheep according to breed, age, sex and season (Die Abhängigkeit der Schilddrüsenausbildung von Rasse, Alter, Geschlecht und Jahreszeit bei verschiedenen Schafrassen). Spöttel, W., Ztschr. f. Anat. p. Entwcklngsg. **89**: 606. 1929.

The relative weight of the thyroid varies greatly in different breeds. In general the male has a larger thyroid than the female. The effect of castration varies with age and breed. The effect of pregnancy is also variable—the gland usually becomes darker in color and more pulpy in consistency. The thyroid is only about half as large in summer as in winter. The histological structure is described in these various conditions. In the spring, especially in March, there is evidence of follicular degeneration. The histological structure of the epithelium indicates greater secretory activity in the winter than in the summer. The method of formation of new follicles is described. The seasonal variation in secretory activity is apparently largely due to tempera-

ture changes, although seasonal variations, especially in light and food, may be contributing factors. The hypofunction of the thyroid beginning in the spring and the hyperfunction which commences in the fall are probably factors in regulating the growth of wool. These and other observations on the sheep are compared with those reported for other animals.—A. T. R.

Exophthalmic goiter. Thompson, W. O. and Bernice Alexander, Arch. Int. Med. **45**: 122. 1930.

In tests on 15 subjects, it was found that the concentration of protein in the cerebrospinal fluid was within the lower limits of normal in most cases of exophthalmic goiter, and usually showed a well marked increase, in association with a gain in weight and reduction in basal metabolism, following a subtotal thyroidectomy.—R. G. H.

The range of effective iodine dosage in exophthalmic goiter. Thompson, W. O., A. G. Brailey, Phebe K. Thompson and E. G. Thorp, Arch. Int. Med. **45**: 261. 1930.

During the daily administration of 1 drop of compound solution of iodine (about 6 mgm. of iodine) to 17 unselected hospital patients with exophthalmic goiter, 15 showed a reduction of 15 to 49 points in basal metabolism, and 2 showed no change. The reduction appeared to be as great as that noted by other observers on much larger doses. A maximum decrease in basal metabolism also appeared to occur in most out-patients during the administration of 1 drop daily. In the house patients, the administration of 1 drop daily caused a maximum reduction in basal metabolism in 7 days on the average. The time that elapsed between the beginning of iodine administration and the onset of a decrease in basal metabolism varied from one to four days. In 5 of the cases it had started within 24 hours after administering only 6 mgm. of iodine. The doses of iodine used at present in the routine pre-operative and post-operative treatment for exophthalmic goiter are probably needlessly large. It is doubtful if more than 5 drops of compound solution of iodine daily is ever necessary to produce a maximum effect. In comparing the effects of various doses of iodine, it is essential to secure a resting level of basal metabolism before medication is begun.—Authors' Summary.

The range of effective iodine dosage in exophthalmic goiter. II. The effect on basal metabolism of the daily administration of one-half drop of compound solution of iodine. Thompson, W. O., E. G. Thorp, Phebe K. Thompson and A. C. Cohen, Arch. Int. Med. **45**: 420. 1930.

During the administration of ½ drop of compound solution of iodine (3 mgm. of iodine) daily to twenty unselected hospital patients with exophthalmic goiter, thirteen showed a significant reduction in basal metabolism, five showed no change and two showed an increase. Seven showed a lower level of basal metabolism during the subsequent administration of 30 drops daily than during the administration of ½ drop daily. The average reduction in basal metabolism during the administration of ½ drop of compound solution of iodine daily was 14 points (from plus 40 to plus 26 per cent)—which was only about half as great as that during the administration of 1 drop daily. The total decrease in metabolism from all doses of iodine was less than in the 1 drop series. In the thirteen cases that responded, the maximum reduction in basal metabolic rate appeared on the average in seven days. In four cases a reduction occurred within twenty-four hours. The daily oral administration of 3 mgm. of iodine in the form of compound solution of iodine is inadequate to produce a maximum reduction in basal metabolism in most cases of exophthalmic goiter in Boston, whereas 6 mgm. is adequate.
—Authors' Summary.

Studies in reactions of simple goiter to iodine. Webster, B., Bull. Johns Hopkins Hosp. **45**: 215. 1929.

Potassium iodide in quantities of 5, 2.5 and 1.25 mgm. was injected intraperitoneally into rabbits with simple goiter (struma diffusa parenchymatosa type) and the changes in heat production were studied and correlated with

the histological changes produced in the gland, as determined by biopsy. The quantity of thyroid hormone elaborated, as indicated by changes in heat production, appeared to vary directly, within certain limits, with the amount of available iodine, as did the extent of involution produced in the gland. This relationship apparently held true until involution was nearly complete. A possible explanation for this phenomenon is suggested.—Author's Abstract.

Lymphadenoid goiter and its clinical significance. Williamson, G. S. and I. H. Pearse, with a note on its etiology in rats by R. McCarrison, Brit. M. J. **1**: 4. 1929.

Histological evidence suggested that the thyroid had 2 functions, (1) the production of the secretion proper (lymphogenic function) and (2) the accumulation of Iodo-colloid. The normal secretory process causes reticulo-endothelial activity of the thyroid as well as an increase of lymphocytes in the interfollicular lymph spaces (lymphogenic secretion). Disturbances of this function give rise to lymphadenoid goiter in which lymphocytes infiltrate the thyroid lymph spaces. Later parenchymal hpyerplasia results in the formation of islands of solid epithelial tissue in the follicular spaces. As the process advances the lympocytic infiltration becomes diffuse and little colloid is present. Atrophy follows exhaustion of the glandular epithelium. At the same time fibrosis of the reticulo-endothelial tissue gives rise to fibrous whorls. Utimately the "woody" thyroid or the gland of myxoedema may result. Thyroid lymphogenesis is the cause of gland atrophy and a progressive hypothyroidism, but is essentially due to a disturbance of lymphogenic function of the gland.

—Wm. Susman.

The importance of the thyroid gland for the nervous activity of animals. Zavadovsky, B., Am. J. Physiol. **90**: 567. 1929.

Hyperthyroidisation with large single doses in chickens and in dogs revealed a double phased action—degradation and disappearance of the conditioned reflexes in the first days after feeding with thyroid gland, and increase of nervous excitability and return of the conditioned indices beginning with the third to fifth day. When fed with small doses of the thyroid gland daily a general increase of the conditioned indices was observed whereas all the reactions become more exact, including the differentiation reaction. Simultaneous study of the unconditioned salivary secretion did not allow interpreting the effect of the experiments as a mere increase of excitability of the peripheral apparatus of the salivary gland but indicated some immediate changes in the activity of the brain cortex brought about by hyperthyroidism. In two dogs with fully established conditioned salivary reflexes the thyroid glands were entirely removed and changes brought about in the conditioned reflex activity of the animals were systematically followed in the course of 8 or 9 months up to the death of the animals, which was caused by cachexia. A sharp decrease of the reflex indices was noted together with a lengthening of the latent period and diminution in the quantity of the secreted saliva; all these changes began on the second month after the operation and reached about 50% of their initial value.—M. O. L.

The influence of the acetyl derivative of thyroxin on moulting and decolorization of hens' feathers (Uber den Einfluss der Azetylderivate des Thyroxins auf die Mauser und Depigmentierung des Hünergefieders). Zawadowsky, B., A. Titajeff and S. Faiermark, Endokrinol. **5**: 416. 1929.

The purpose of the experiment was to determine which parts of the thyroxin molecule caused the moulting and decolorization of feathers which the authors had, in an earlier series of experiments, shown to be a result of administration of the thyroid hormone. The substances tested were the original (keto) form of thyroxin, the open-ring form, and the acetyl derivatives of both of these compounds. Injections of alkaline solutions of the four substances were given subcutaneously to black hens. In the case of the keto and open-ring forms, and the acetyl derivative of the latter, injections were followed first by moulting, and later by growth of white feathers in the region around the site of the injection. The acetyl derivative of the keto form pro-

duced but little effect. Diiodotyrosin, given in large doses, had no effect. The authors discuss especially the slight reaction of the hens to acetyl derivative of the keto form. They compare the effect this has on the plumage of hens with amphibian metamorphosis on the one hand and metabolic changes on the other, apparently regarding all three reactions as essentially similar. Since this form of acetyl thyroxin accelerates amphibian metamorphosis, produces but little change in plumage, and has no effect on the metabolic rate in mammals, they conclude that birds stand midway between amphibia and mammals in the type of iodine compounds to which they respond. They suggest that the effect on plumage may be used as a test in comparative studies of thyroxin and its derivatives.—M. M. H.

A biological method for estimation of thyroid activity (Eine biologische Methode zur Bestimmung der Schilddrüssen-Aktivität bei Tieren). Zawadovsky, B. and M. Nowikova, Endokrinol. **1**: 167. 1928.

A research was carried out on 107 Axolotls in which were implanted grafts of thyroid from chickens, dogs, cats, rabbits, guinea-pigs and doves. This method permits an evaluation of the efficacy of the thyroid tissue in terms of its metamorphosis-inducing properties. It was found that 30 mgm. was the minimal and 50 mgm. the optimal dosage for Axolotls weighing 4-10 grams. Thyroid tissue from various species proved to be about equally efficacious, that from hens had greatest potency.—R. G. H.